

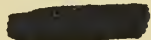
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SEMINAR TOPICS

I Semester 1936-37

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VITAMIN D

- A. Windaus and W. Thiele, Ann., 521, 160 (1935)
A. Windaus, Lettre and Schenck, ibid., 520, 98 (1935)
A. Windaus, Schenck and Werder, Z. physiol. Chem.,
241, 100 (1936)
H. Brockman, ibid., 241, 104 (1936)

Located at: University of Gottingen

Earlier Work: Natural Products

Rickets, a disease of childhood and characterized by improper ossification, is intimately connected with a Vitamin D deficiency in the body.

In contributing to the relief of the disease two methods have been resorted to, (a) exposure to sunlight and (b) the administering of cod liver oil.

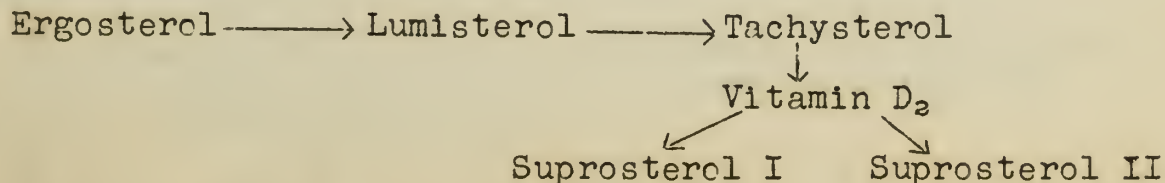
Further investigation of the active principle of cod liver oil led to the fact that the antirachitic principle was to be found in the oil soluble non-saponifiable part.

Since the physiological importance of Vitamin A was receiving much attention the disease of rickets was also thought to be due to a deficiency of this vitamin. Feeding experiments together with the fact that an inert oil only showed antirachitic properties when irradiated, convinced observers that the antirachitic principle of cod liver oil was not Vitamin A.

Cholesterol was then thought to be the pro-vitamin of Vitamin D but later it was found that an impurity, ergosterol, was the real pro-vitamin.

Observers in England and Germany independently obtained a crystalline product from irradiated ergosterol which showed curative properties towards rickets. This was called Vitamin D₁. A short time later this crystalline material was shown to be a molecular compound of the Vitamin and an inactive isomer lumisterol. In 1932 the pure active principle was isolated and called Vitamin D₂ by Windaus and his coworkers. Vitamin D₂ was found to be different from the naturally-occurring Vitamin found in tunny fish liver oil. This naturally-occurring vitamin has been isolated recently and is called Vitamin D₃.

Five successively different crystalline compounds were obtained from irradiated ergosterol. This may be represented in the following way,



1. The first part of the report is devoted to a description of the work done during the last year.

2. The second part is devoted to a description of the work done during the last year.

3. The third part is devoted to a description of the work done during the last year.

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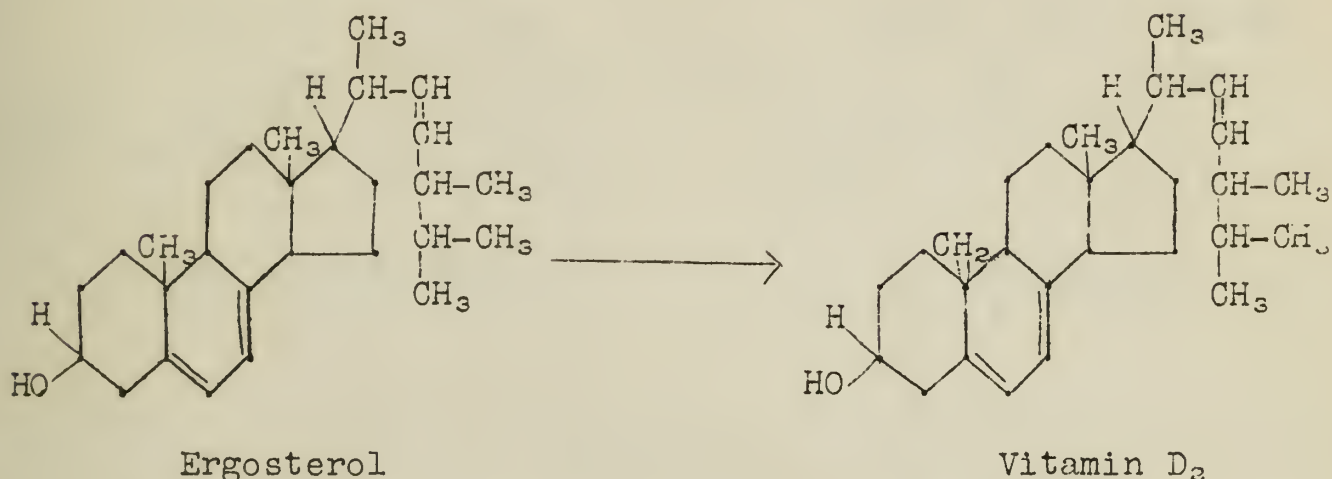
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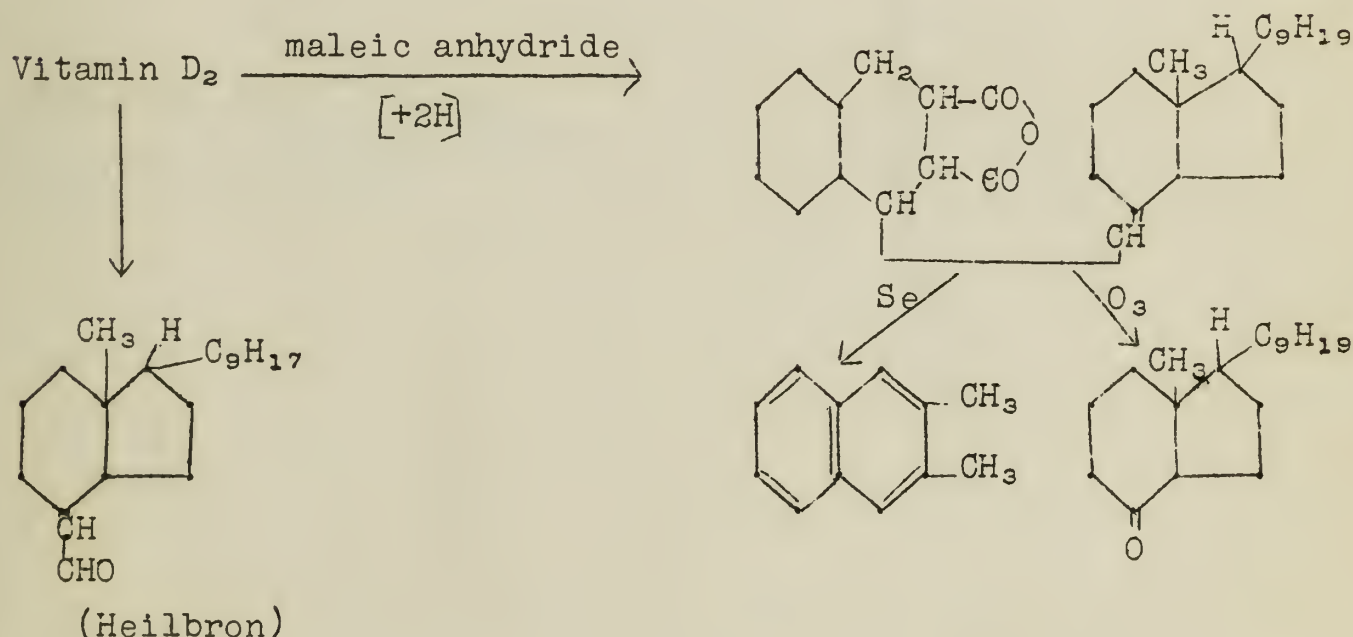
13. The thirteenth part is devoted to a description of the work done during the last year.

-2-

Windaus concludes that the following formula for Vitamin D₂ obtained from irradiated ergosterol may be represented thus:



These conclusions have been deduced from the following reactions:

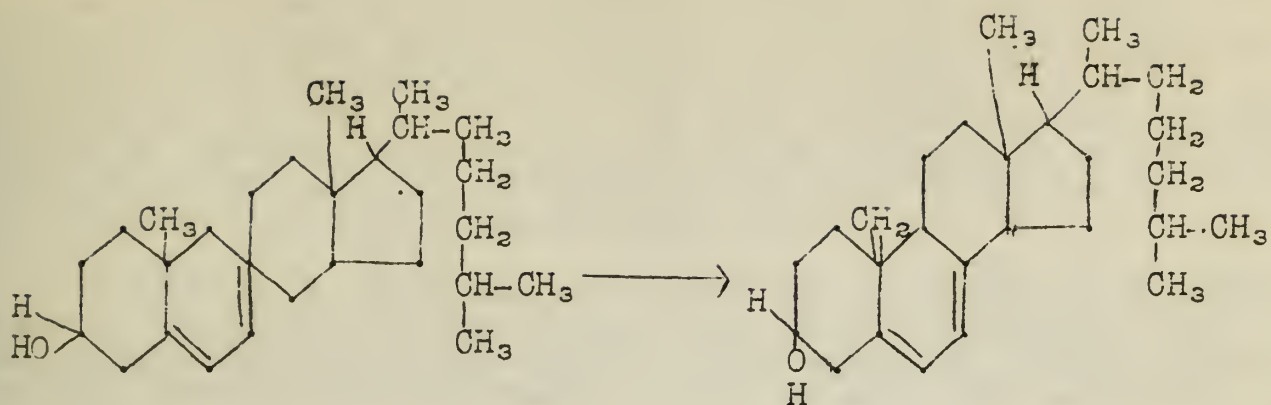


Windaus obtained other compounds that also showed anti-rachitic properties on irradiation; 22-dihydroergosterol which is ergosterol with the side chain hydrogenated and 7-dehydrocholesterol.

Brockman isolated the natural vitamin from the tunny fish liver oil and found this to be identical with the irradiated 7-dehydrocholesterol.

Windaus suggests the following formula for Vitamin D₃ from irradiated 7-dehydrocholesterol.

-3-

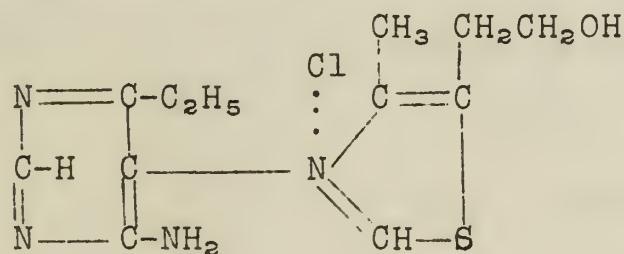
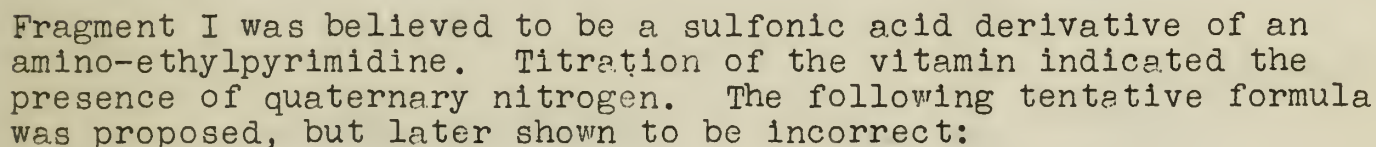
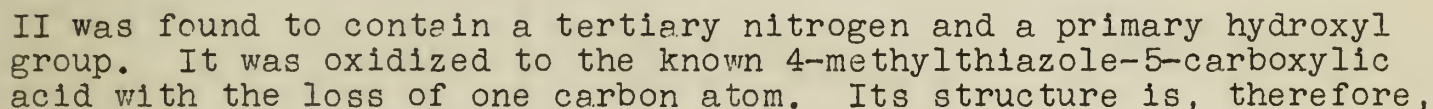


7-dehydrocholesterol

Vitamin D₃

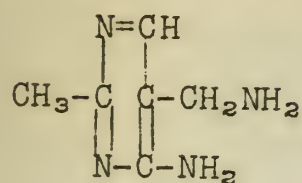
Reported by R. C. Morris
G. E. Eilerman
September 30, 1936.

In 1934 R. R. Williams and coworkers described an improved method of isolation of the vitamin from rice polishings. (3a) With its aid they obtained sufficient amounts for study. Early in 1935 they reported the cleavage of the vitamin with sulfurous acid. (3b)


$$\begin{array}{c} \text{N}=\text{CH} \\ | \\ \text{CH}_3-\text{C}-\text{C}-\text{CH}_2\text{SO}_3\text{H} \\ || \quad | \\ \text{N}-\text{C}-\text{NH}_2 \end{array} \xrightarrow{[\text{H}]} \begin{array}{c} \text{N}=\text{CH} \\ | \\ \text{CH}_3-\text{C}-\text{C}-\text{CH}_3 \\ || \quad | \\ \text{N}-\text{C}-\text{NH}_2 \end{array}$$

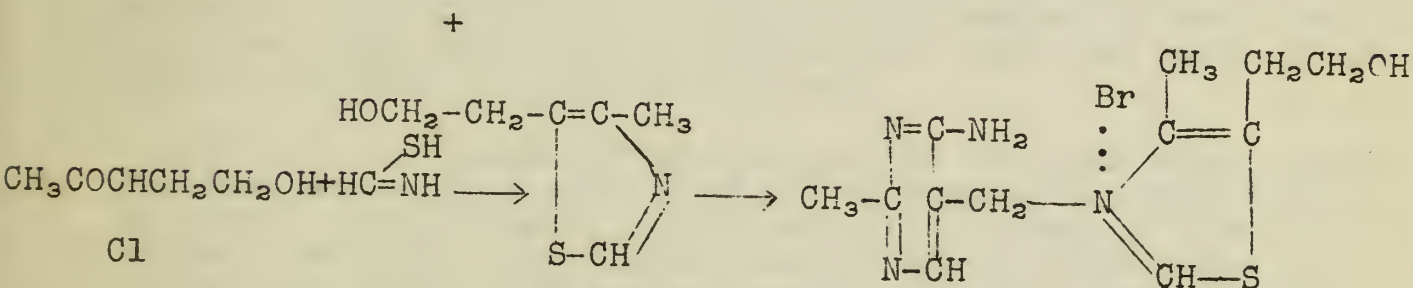
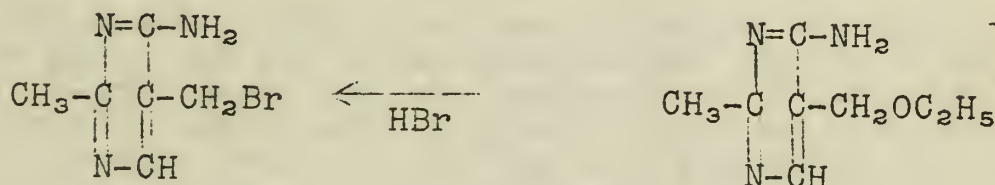
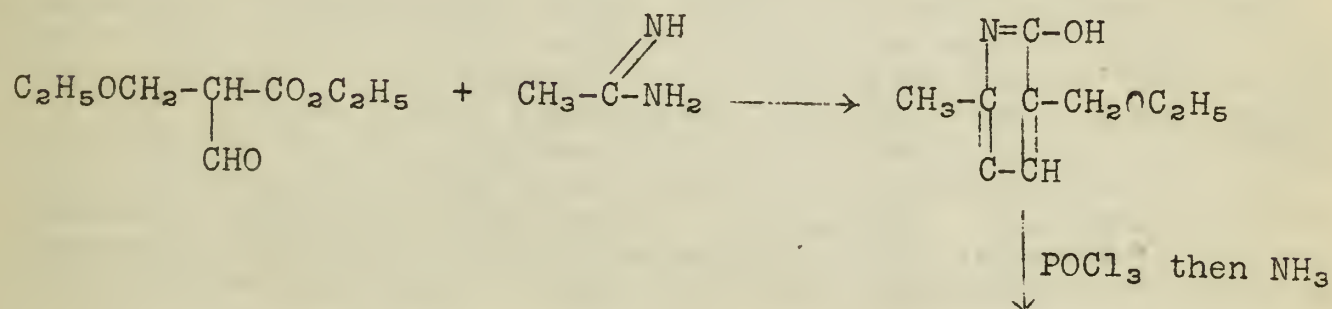
The identity of the pyrimidine portion of the molecule was independently proven by Grewe(4) in August 1936. By catalytic reduction of the product of condensation of acetamidine and ethoxymethylmalononitrile he obtained a diaminopyrimidine identical

with a diamine previously obtained by himself and Windaus(3)



by permanganate oxidation of the vitamin.

The synthesis of Vitamin B₁ by Williams and Kline(3a) follows:



Vitamin B₁

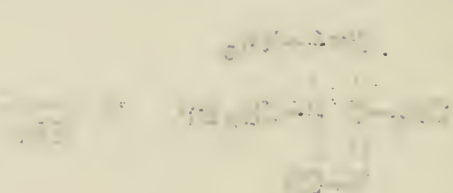
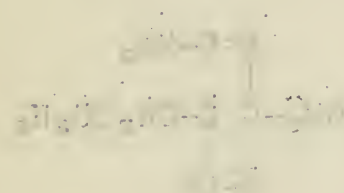
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1. Outlines of Biochemistry, R.A. Gortner, John Wiley and Sons(1929)
2. Windaus et al (Goettingen), Z. physiol.chem., 204,124 (1932); 228,27(1934); 237,98 (1935)
3. R.R.Williams (Bell Tel. Lab.), H. T. Clark, S. Gurin et al, J. Am. Chem. Soc., 56, 1187 (1934); 57, 229, 536, 1876(1935); 58, 1063, 1504 (1936)
4. Grewe, Z. physiol. chem., 242, 89 (1936)
5. Buchman, J. Am. Chem. Soc., 58, 1803 (1936)

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VITAMIN B₂

Richard Kuhn and coworkers, Ber., 69, 2034 (1936)

(Kaiser Wilhelm Institute, Heidelberg)

Paul Karrer and coworkers, Helv. Chim. Acta, 19, 483 (1936)

(University of Zürich)

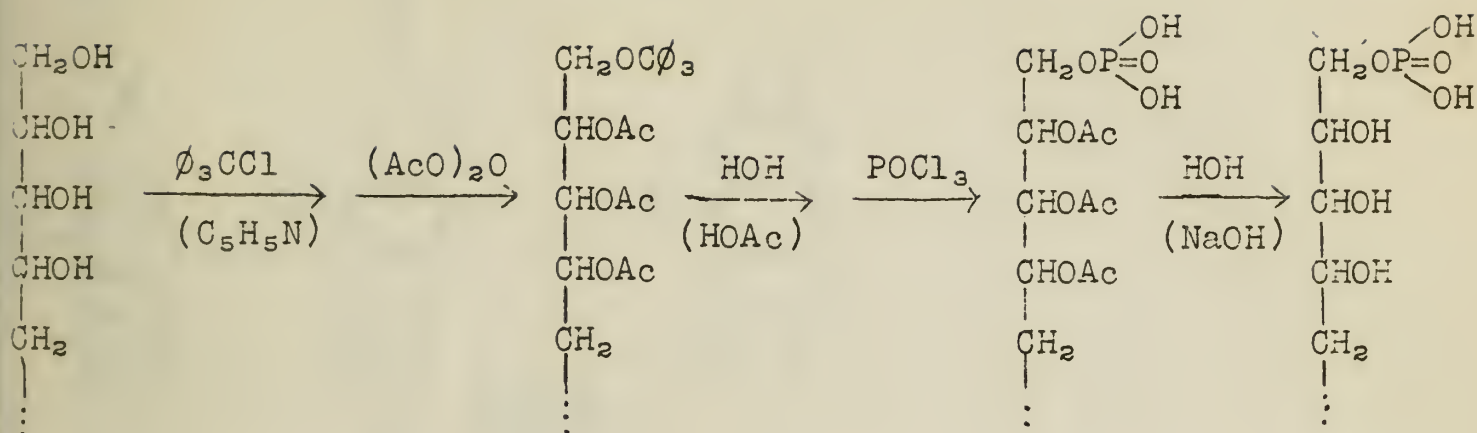
In 1926 it was recognized that Vitamin B was not composed of a single factor but that one, Vitamin B₁, was responsible for antineuritic properties, while Vitamin B₂ was assigned growth-promoting properties as well as ability to cure pellagra. With the isolation of crystalline lacto- and ovo-flavine (identical) in 1933 by Kuhn it was discovered that this compound was partly responsible for the growth-promoting properties accorded Vitamin B₂. Consequently, the term Vitamin B₂ is now applied to the chemical compound lacto-flavine, C₁₇H₂₀N₄O₆. A summary of the important reactions used in determining its structure are outlined below (all Kuhn's work except the discovery of lumichrome).

After the proof of the structural formula, the configuration of the side-chain had yet to be determined. Kuhn's first guess was that of L-arabinose, but his synthesis of 6,7-dimethyl-9 (L-1'-arabityl)-isoalloxazine yielded a compound differing in physical properties from, and having only one-third the activity of natural lacto-flavine. Kuhn and Karrer then simultaneously announced that the synthetic D-ribityl derivative was completely identical with the natural product not quite two years after its first isolation in crystalline form.

Karrer, by synthesis of four of the six remaining stereoisomers, as well as some twenty-five similarly constituted flavines, was unable to obtain any other compound showing vitamin activity. Apparently, due to steric hindrance, no structural isomers of lacto-flavine with the methyl groups in any but the 6,7-positions could be obtained. An interesting observation by Kuhn in this respect is that 6,7-dimethyl-alloxazine has a lower oxidation-reduction potential than any of its isomers or homologs.

A "yellow oxidation enzyme" discovered by Warburg and Christian is able to effect a transfer of oxygen in aerobic cells or to be an enzyme for respiration in the absence of oxygen in anaerobic cells. It was reversibly decomposed by Theorell to a colloidal "carrier" and a lacto-flavine-phosphoric acid. Kuhn has shown the latter to be the 5'-derivative:

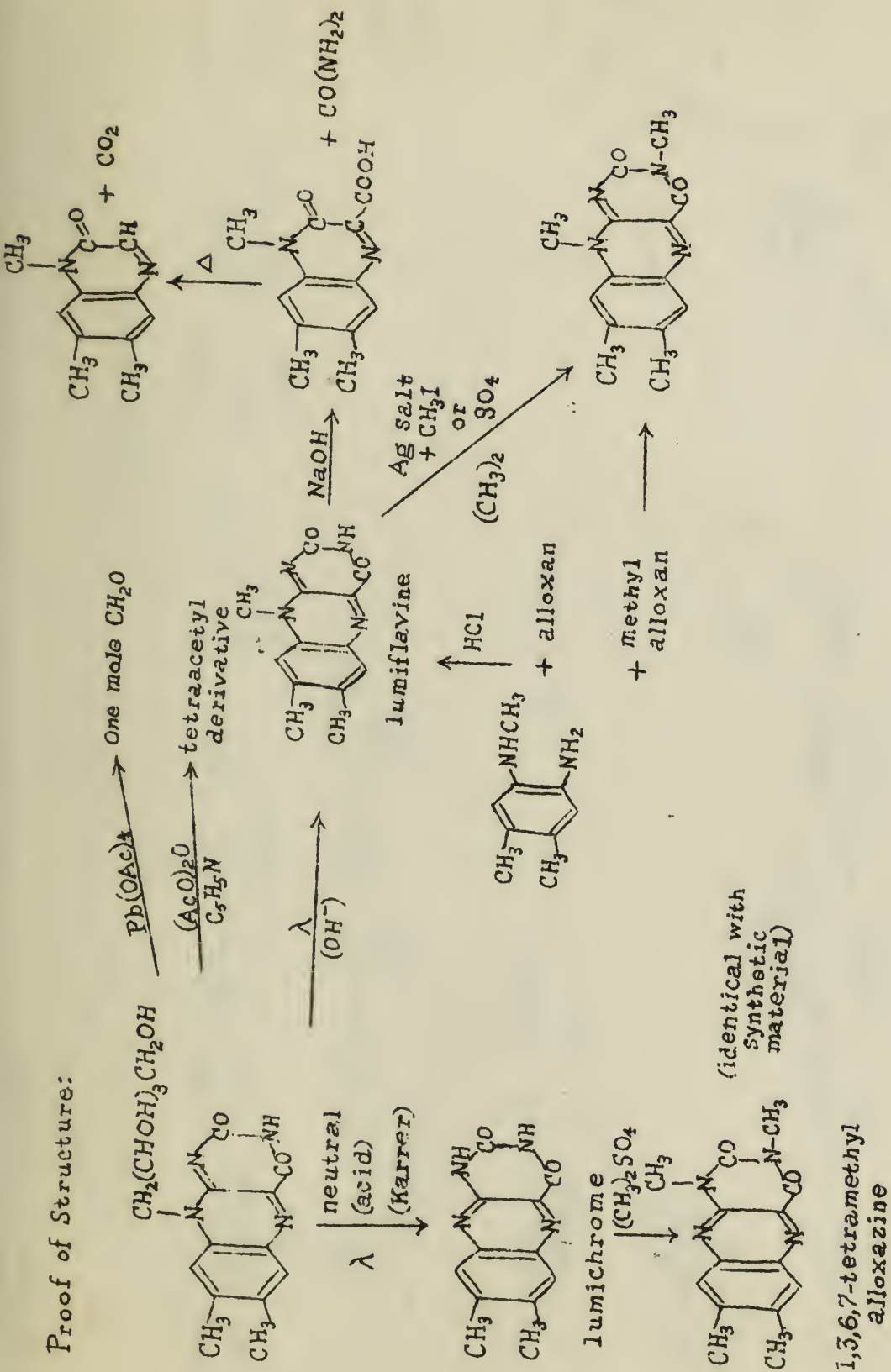
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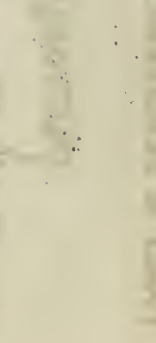
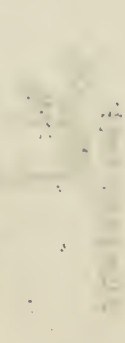
Very recent work by Kuhn has shown that both synthetic lacto-flavine and its arabityl isomer may be combined with the natural carrier with the formation of an active enzyme.

Reported by C. C. Price
 Harry Sutherland
 October 14, 1936.

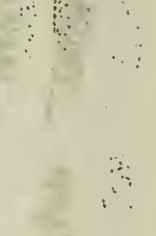
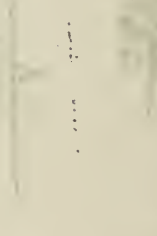
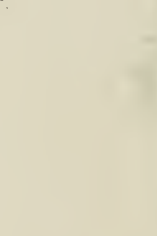
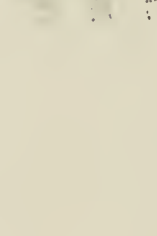
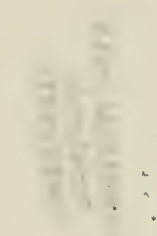
Proof of Structure:



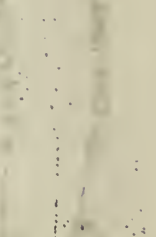
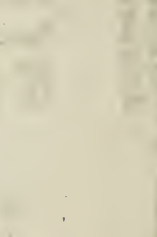
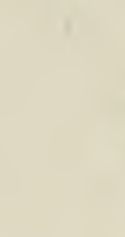
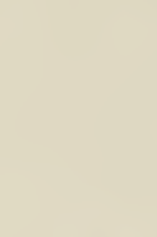
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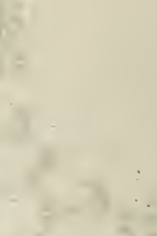
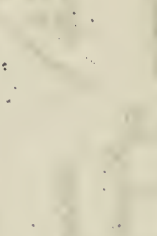
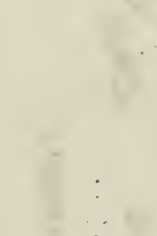
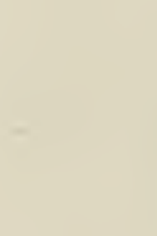
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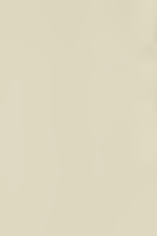
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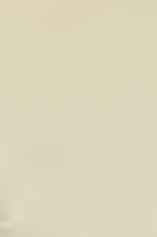
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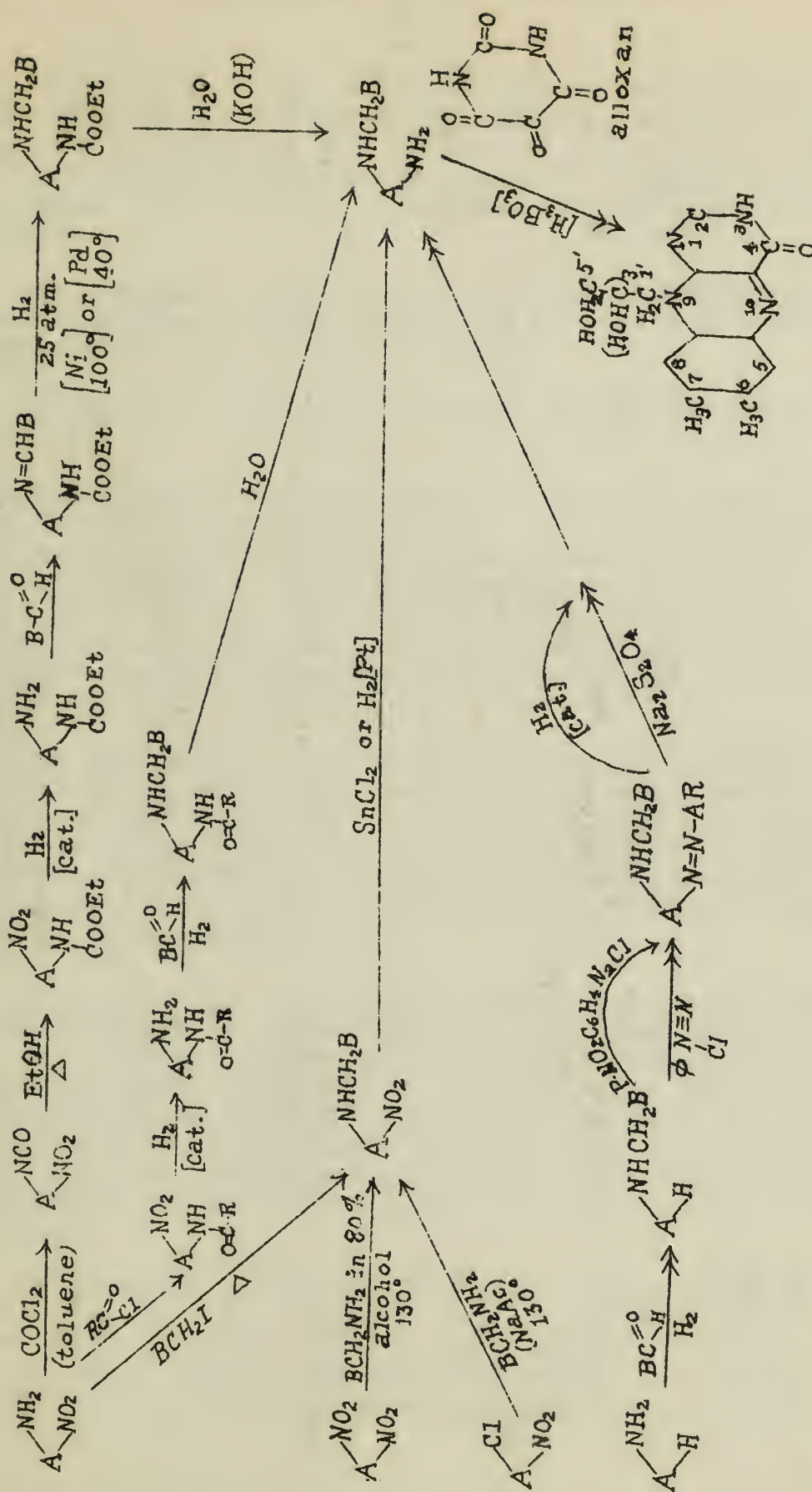
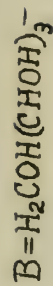
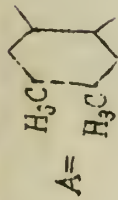


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Syntheses of Flavines:



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ANDROSTERONE AND TESTOSTERONE

It has been shown that all sexual processes are controlled by certain chemical substances known as sex hormones. The hormones are secreted by the testes or the ovaries under the stimulation of hormonal secretions from the anterior lobe of the pituitary. The pituitary hormones are called gonadotropic hormones.

The commonest method used for the quantitative bio-assay of androsterone is that depending on its influence on the development of comb growth in capons.

The first isolation of a male hormone was done by Butenandt in 1931 in the investigation of the urine of males.

Structure of androsterone: $C_{19}H_{30}O_2$. Androsterone was found to be completely saturated. Androsterone gives an acetate whose analysis corresponds to the formula $C_{19}H_{30}O_2$ or $C_{18}H_{28}O_2$ (for the hormone). Both formulas would indicate a carbon skeleton of four reduced rings, containing one ketonic and one hydroxyl group. On the basis of analogy with oestrone (2), Butenandt in 1932 suggested what has proved to be the correct formula for androsterone (1).

The analysis of the acetate would not distinguish whether a methyl group which was assumed to be a C_{10} was present or not. If this methyl group were not present then androsterone would differ from oestrone (2) only by the amount of hydrogen in Ring A. However, Schoeller, on hydrogenation of oestrone, obtained a compound which, while physiologically similar, was not identical with androsterone.

At about this time (1934) Ruzicka attempted the preparation of androsterone by the oxidation of dihydrocholesteryl acetate (3). He isolated a product of expected composition but less active and also differing in melting point from androsterone. It was suggested that the two compounds were stereoisomers. Oxidation of epicholesteryl acetate (3a) (a stereoisomer which has a different configuration of the hydroxyl on C_3) gave androsterone. Marker, in 1935, used the following improved synthesis.

Cholesterol $\xrightarrow{PCl_5}$ cholesteryl chloride $\xrightarrow[\text{Pt}]{H_2}$ dihydrocholesteryl chloride $\xrightarrow{CrO_3}$ α -chloroandrosterone \xrightarrow{KAc} androsterone. Since androsterone has an opposite configuration to cholesterol at C_3 an inversion must have occurred in one of the steps.

Ruzicka found that the oxidation of the dibromcholesteryl acetate gave better yields and the correct stereoisomer, i.e., androsterone.

CONFIDENTIAL

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Dehydroisoandrosterone: There was also isolated from the urine two substances, of which one is an unsaturated chloro-ketone, probably formed by the action of hydrogen chloride on an unsaturated hydroxy compound. The second was an unsaturated hydroxy compound (6).

The chloro compound (4) by conversion to the benzoate and hydrolysis was converted into the hydroxy compound (6). The chlorocompound (4) by hydrogenation, conversion to the acetate and hydrolysis produced androsterone (1). Dehydroisoandrosterone (6) was synthesized by Ruzicka by the following series of reactions: cholesterol $\xrightarrow{\text{acetylate}}$ cholesterol acetate $\xrightarrow{\text{Br}_2}$ cholesterol acetate dibromide $\xrightarrow{\text{CrO}_3}$ dehydroisoandrosterone dibromide $\xrightarrow[\text{Zn}]{-\text{Br}}$ dehydroisoandrosterone.

This synthesis establishes the structure of dehydroisoandrosterone (6), and shows that the configuration of the hydroxyl on C₃ is different in androsterone and dehydroisoandrosterone, hence, the "iso" in the latter name.

At about this time Butenandt converted α -chloroandrosterone (7) into androstenone (8) and this could be hydrogenated to androstanone (9). Ruzicka then oxidized cholestane (10) to a product identical with androstanone (9). This proved independently the structure of androsterone except for the position of the hydroxyl group.

It was at first believed that the testicular hormone might be identical with the urinary hormone, androsterone. However, physiological differences were noted by Laquer at Amsterdam, and chemical differences by Gallagher at Chicago.

The crystalline material was first isolated by Laquer from testis tissue in June, 1935. From its physiological and chemical properties both Butenandt at Danzig and Ruzicka at Zürich were led to believe it was Δ^4 -androstrenecne-3-ol-17. Both investigators synthesized this compound by the same method, and the independent results were announced within three days of each other in September, 1935. Later, Ruzicka improved the yield by a modification of the synthesis.

The original method consisted in the reduction of (6) to (11) by sodium and propyl alcohol and the conversion of this to the diacetate. Since the 3-substituent is more active, partial saponification yields (12). This was oxidized as the dibromide, and the product on debromination and hydrolysis gave (13). This is identical chemically, physically and physiologically with testosterone isolated from testis tissue.

THE UNIVERSITY OF CHICAGO
DEPARTMENT OF CHEMISTRY
CHICAGO, ILLINOIS 60637

TO THE EDITOR:
I am writing to you to inform you of the results of my research on the properties of the new material I have discovered. The material has been found to have a unique set of properties that make it a promising candidate for a variety of applications.

The material is a new type of polymer that has been synthesized from a novel process. It has a high degree of stability and is resistant to degradation. It also has a high degree of flexibility and is easy to process. These properties make it a very attractive material for a wide range of applications.

I have conducted a series of experiments to determine the properties of this material. The results of these experiments are as follows: The material has a high degree of stability and is resistant to degradation. It also has a high degree of flexibility and is easy to process. These properties make it a very attractive material for a wide range of applications.

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Ruzicka's improvement was the preparation of the acetate-17-benzoate (14), which, on partial saponification yields the 17-benzoate. From this point on the syntheses are identical.

Later work has been concerned with the physiological action of derivatives. In particular, 17-methyl testosterone, known only from synthesis, is even more active than testosterone.

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(Schering-Kahfbaum-A.G.)

Reported by C. E. Denoon, Jr.

C. L. Fleming

October 21, 1936.

1. *Chrysomelidae* (Coleoptera)
2. *Curculionidae* (Coleoptera)
3. *Chrysomelidae* (Coleoptera)

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FEMALE SEX HORMONES AND RELATED SUBSTANCES

Butenandt - University of Göttingen
 Doisy - St. Louis University, School of Medicine
 Robinson - Dyson Perrins Laboratory, Oxford University
 Cohen, Cook, Hewett - Research Institute of the
 Cancer Hospital, London
 Haworth - University of Durham, Armstrong College
 Fieser - Harvard University
 Fernholz - University of Göttingen

The female sex hormones, oestrone and progesterone, are secreted by the genital glands under the influence of hormonal secretions from the anterior lobe of the pituitary. They control the growth and physiological functioning of the reproductive organs and promote the development of female secondary sex characteristics.

Oestrone, I, was isolated independently by Doisy and Butenandt in 1929 from human pregnancy urine. The hormone occurs in various other sources, both animal and vegetable, the richest source discovered as yet being the urine of stallions. Methods of isolation take advantage of the stability of the hormone toward acid and alkali, its phenolic character, and its reactivity toward ketone reagents.

Analyses of the compound indicated the formula $C_{18}H_{22}O_2$, and its chemical behavior characterized it as a hydroxy ketone containing one benzenoid ring. X-ray and crystallographic studies by Bernal,¹ led to the conclusion that the hormone was a long molecule with the phenolic and keto groups at opposite ends. Butenandt^{2a} determined by catalytic hydrogenation and molecular refraction that only three double bonds were present. Another compound, $C_{18}H_{24}O_3$, weakly oestrogenic, was isolated from natural sources and Butenandt^{2b} proved this to be a hydrate of oestrone by dehydration to the hormone with $KHSO_4$. The hydrate, II, proved to be susceptible to ring cleavage with KOH and this step opened the way to successful degradation and proof of structure as outlined in the diagram.

That the oestrone structure is not specific for oestrogenic activity is shown by investigations by Cook, Dodds, and Hewett,³ Marker,⁴ and Butenandt.^{2c}

Considerable evidence points to oestrodol (dihydro-oestrone) as the active hormone with respect to the biological function.

A number of workers are attempting the synthesis of oestrus-producing sterol structures.⁵ Haworth's synthesis of IV is representative of these methods.⁶ Marker,⁷ has accomplished a partial synthesis of oestrone from ergosterol.

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As early as 1903 Fraenkel showed that the removal of the corpora-lutea shortly after ovulation terminates pregnancy or prevents attachment of the ovum to the uterus. In 1928 G. W. Corner and W. M. Allen observed that injections of extracts of the corpus luteum restored test animals to normal. Normal conditions of pregnancy in extirpated rabbits could be maintained completely through full term showing conclusively that the internal secretions of the corpus luteum contain a hormone which controls pregnancy.

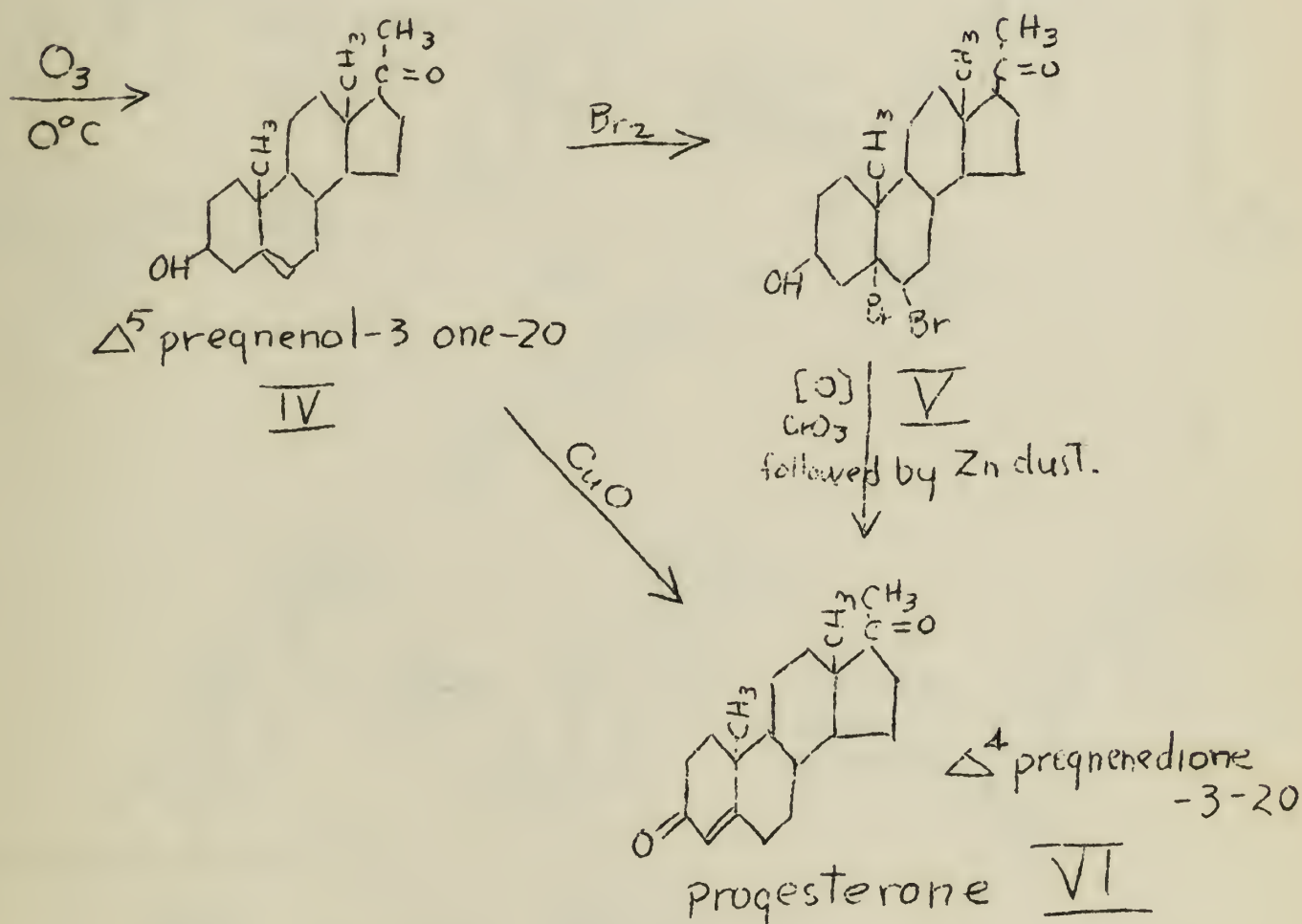
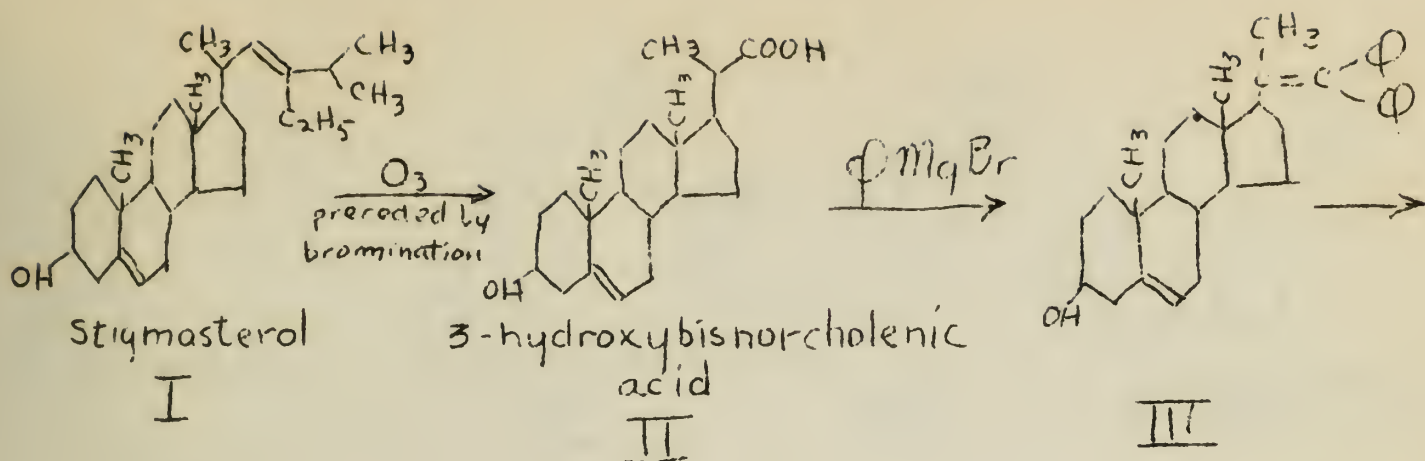
The Corner-Allen method of bio-assay depends on production of characteristic changes in the uterine mucosa of castrated female test animals. The Clauberg test is similar but uses the infantile animal rather than the adult. Both are reproducible and serve as a convenient measure of progestational activity.

During the month of April, 1934, or shortly thereafter, no less than four laboratories announced the isolation of the pure hormone. Two physiological diketones were obtained along with an inactive hydroxyketone. The two diketones were polymorphic and were given the names of alpha and beta progesterone. The common source of progesterone was the sow ovary.

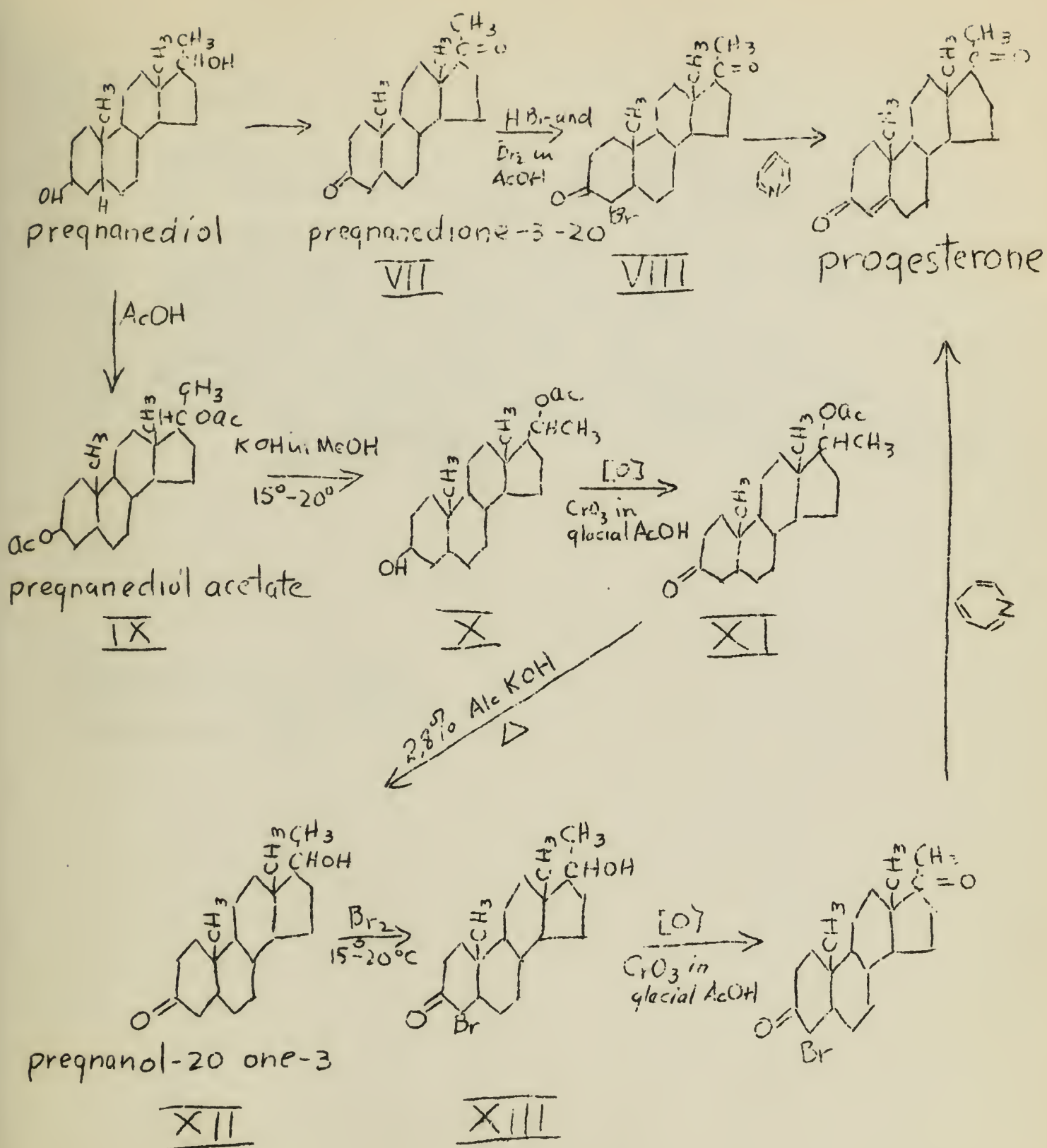
Methods used in extraction of the hormone included long solvent extractions, partitutions, selective absorption, and crystallization. The final purification was through the semi-carbazone.

The empirical formula was determined as $C_{21}H_{30}O_2$. Absorption spectra data indicated an alpha-beta unsaturated compound while X-ray data showed a sterol-like structure. On the basis of the facts on hand Slotta,⁵ in 1934 proposed the structure VI which later proved to be entirely correct.

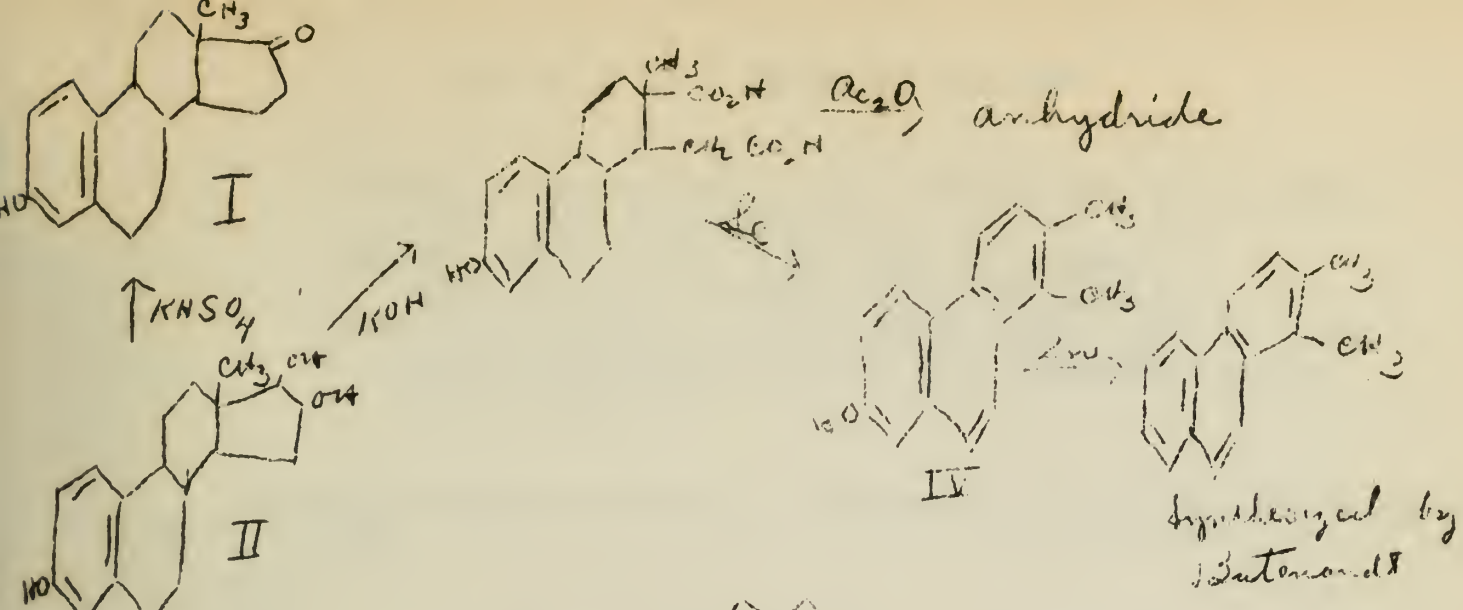
Proof of the structure was based on the above facts and synthesis. In November of the same year isolation of the hormone was announced by Butenandt,^{1,2} and later Fernholz,⁶ reported the successful synthesis of progesteron from stigmasterol.



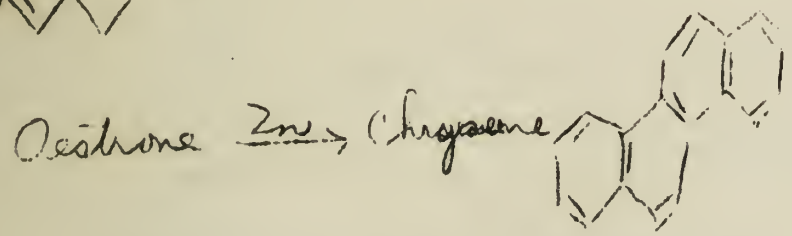
Before complete account of the above work was published Butenandt,² reported a pseudo synthesis using pregnanediol isolated from human pregnancy urine as a starting material. The synthesis was carried out in two ways as indicated in the accompanying diagrams.



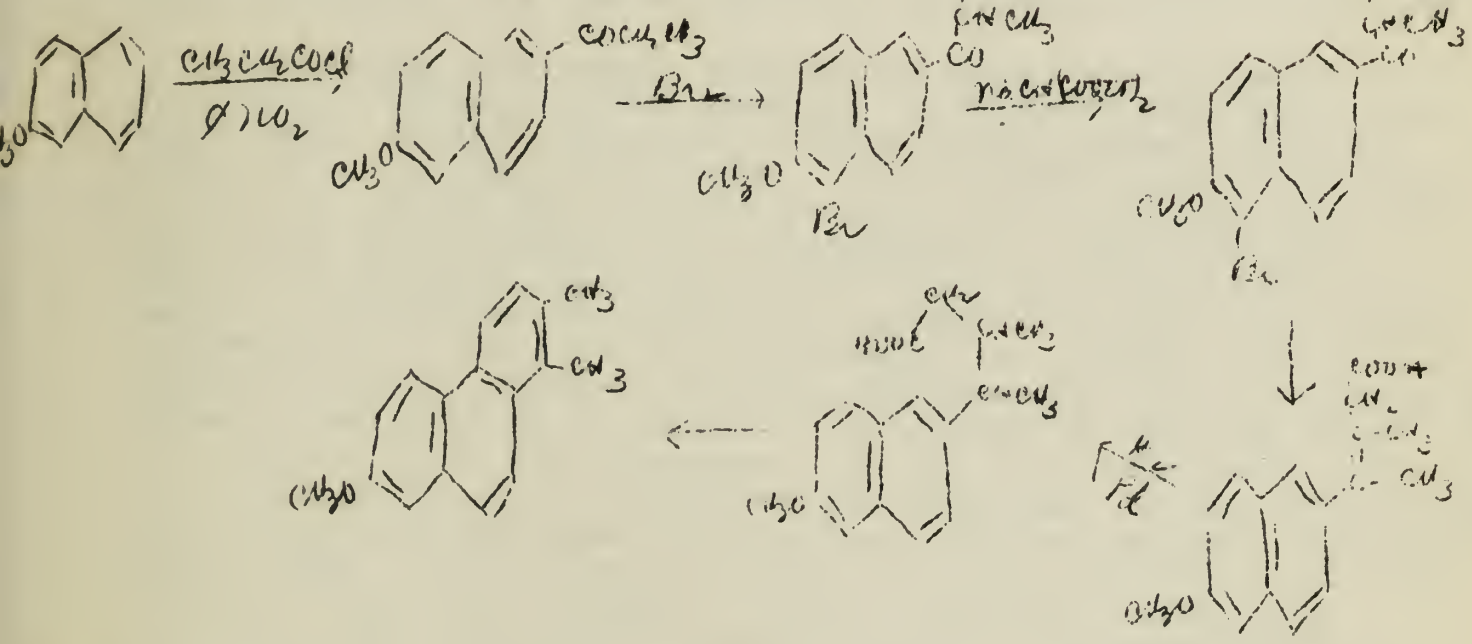
Progesterone is unique among the sex hormones in its specificity. To date no other compound has been observed which will respond to the Corner-Allen or to the Clauberg tests.



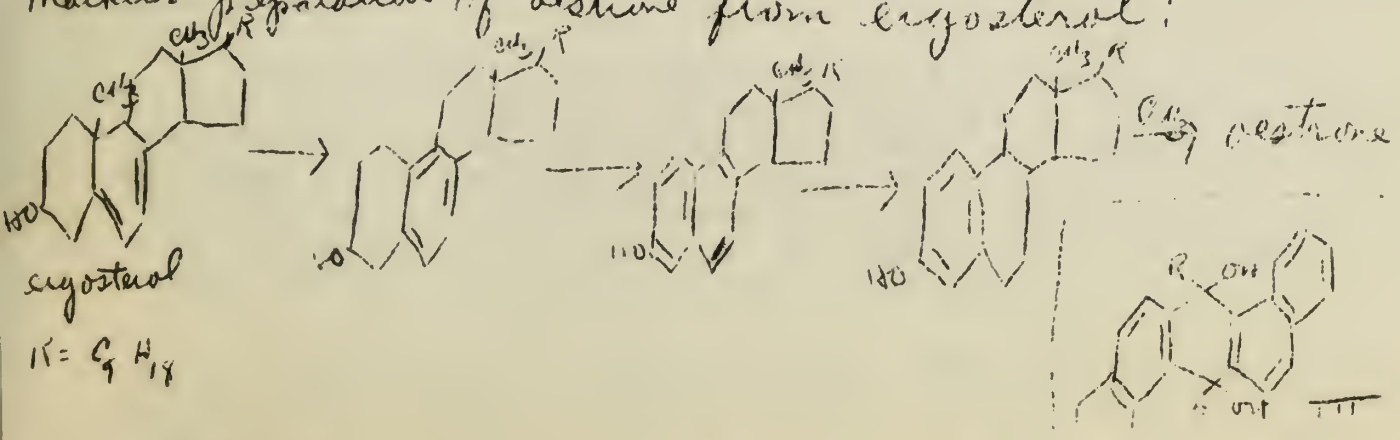
Synthesized by Butenandt



Haworth's synthesis of the Me ether of IV



Markier's preparation of oestrone from ergosterol:



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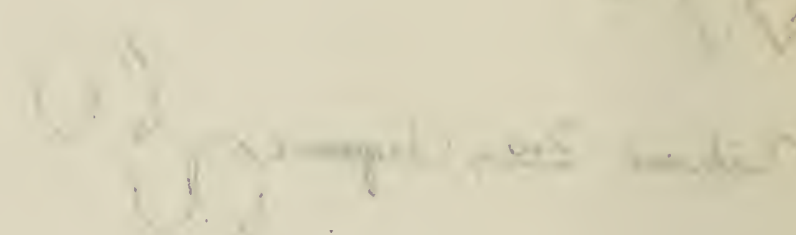


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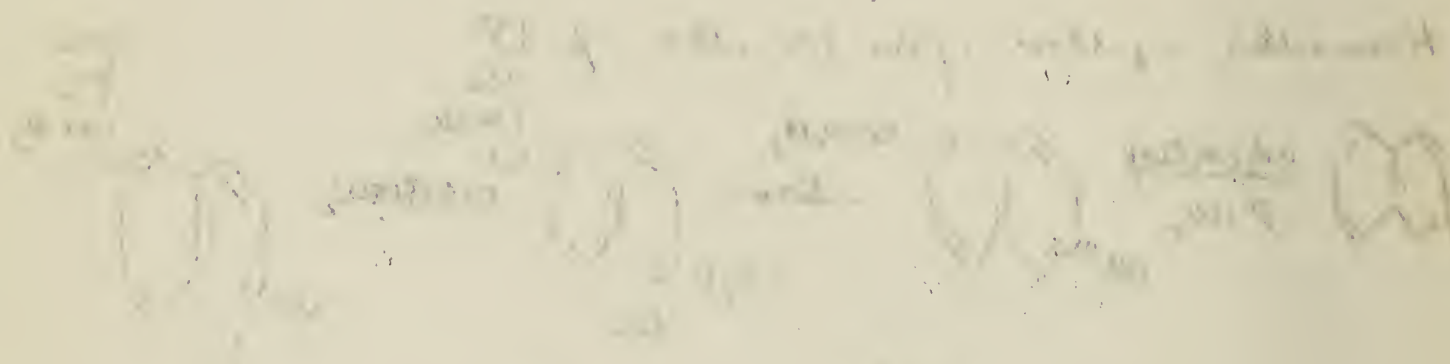
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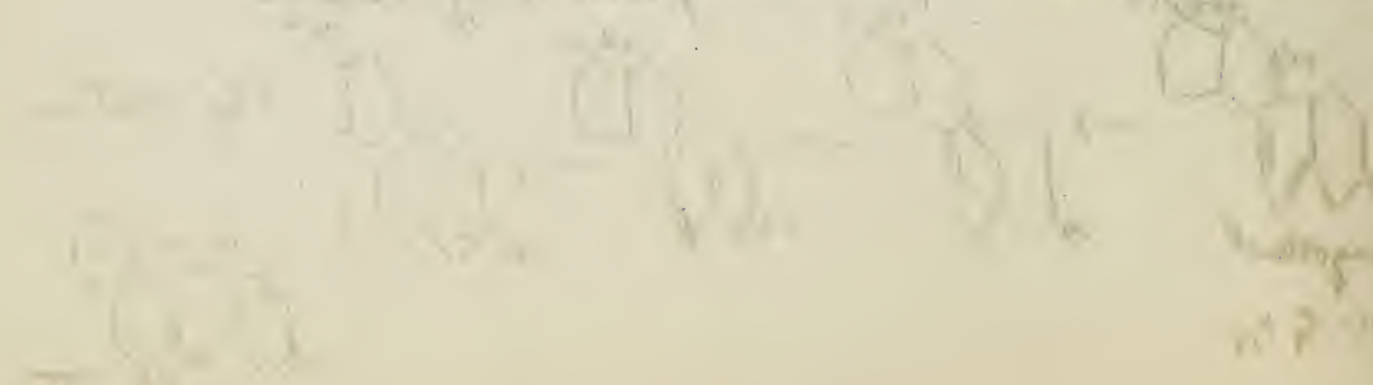
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Karrer, Schwarzenbach, Benz, Solmssen; *Helv. Chim. Acta*, 19, 811 (1936)

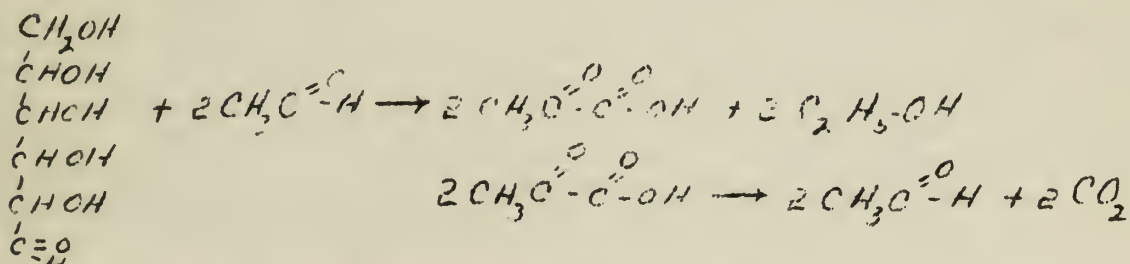
Karrer, *Helv. Chim. Acta*, 19, 33 (1936)

Zürich, Chem. Institut der Universität

Warburg, Christian, *Helv. Chim. Acta*, 19, 79 (1936)

Kaiser Wilhelm Institut für Zellphysiologie,
Berlin-Dahlem

Warburg explains alcoholic fermentation by the following two-step process.



Fermentation is thus the transfer of hydrogens from aldehyde to hexose. This process can be shown to be catalyzed by pyridine by the series of equations marked I. Pyridine itself cannot be used satisfactorily, but a substituted pyridine may be employed.

According to Warburg, the physiological significance of lactoflavin depends on the capacity to transfer hydrogen. Carbohydrates or their phosphoric esters cannot reduce pyridine nucleotides in aqueous solution. If one adds specific proteins, a union of nucleotide and protein takes place in which the pyridine ring can be reduced by carbohydrates. These pyridine-nucleotide-protein compounds are the hydrogen transporting ferment, called Coferment, hereafter designated by Co. The reduced Coferment, Co, can give up its hydrogen in a medium such as the yellow oxidation ferment, and the hydrogenated form of the yellow ferment, called F_H, is finally dehydrogenated again by oxygen to F. See set II of the equations. We are here interested only in that part of Co which transports the hydrogen. Co has been shown to consist of a nicotinic acid amide, adenine, pentose, and phosphoric acid. The active principle, Co, was discovered and isolated at Dahlem by Warburg in 1934. It occurs along with Cozymase, the diphosphopyridine nucleotide, whereas the Co is the triphospho compound. The two occur in nature as "pyridine-nucleotides."

Free nicotinic acid amide cannot be hydrogenated reversibly to the dihydro compound, since Pt-H₂ gives an irreversible hexahydrate and hyposulfite fails to produce any reduction. The two nitrogen atoms and the amide oxygen were substituted in order to find the compound which formed the **active** part of Co, and it was found that the reduced form of the quaternary salt formed with methyl iodide (III) was the active principle.

On reduction with hydrosulfite, the nicotinic acid amide methyl iodide gave a compound which analyzed for C₇H₁₀ON₂; its formula was, therefore, given by IVa, b, or c. From physical properties and from spectral data, IVc, the para compound, is

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 WORK DURING THE YEAR 1900
 THE BOARD OF DIRECTORS
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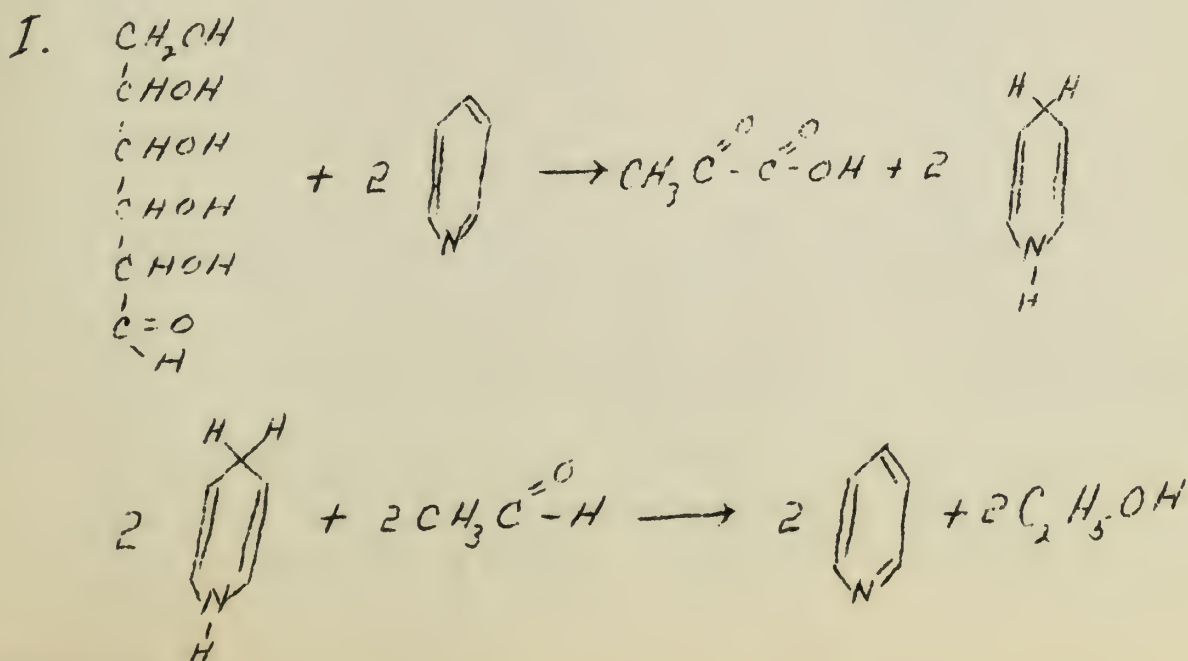
REPORT ON THE PROGRESS OF THE
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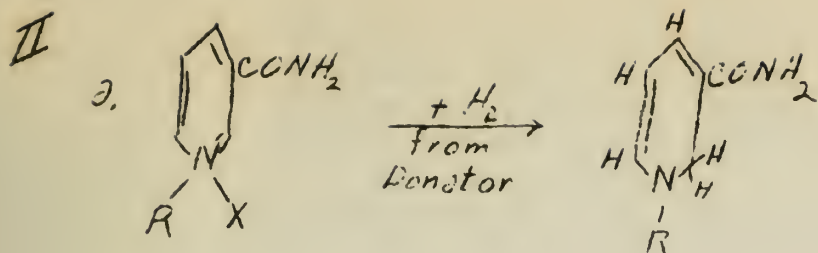
eliminated. The primary reversible reduction product is an extraordinarily strong reducing agent, reducing silver nitrate solution instantly in the cold, decolorizing methylene blue, and indigo tetrasulfonate. It impresses a strong negative potential on a platinum electrode. A secondary reduction product, identified by physical constants and absorption spectra, is the para compound, IVc, which forms to the extent of about ten per cent. It is not known whether this is formed by transformation of the ortho compound or whether the amide can be reduced directly to the para compound.

Dihydro compounds have characteristic absorption bands in the ultra-violet region. All reversible dihydropyridine compounds show white fluorescence in ultra-violet light. One is thus able to observe the formation and disappearance of the dihydro compound in reactions involving the nucleotide and yellow ferment. The active principle, Co, is not auto-oxidizable, while the reduced form of yellow ferment is auto-oxidizable. This is illustrated in series V of the reactions.

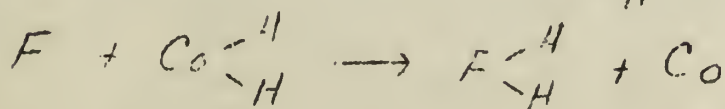
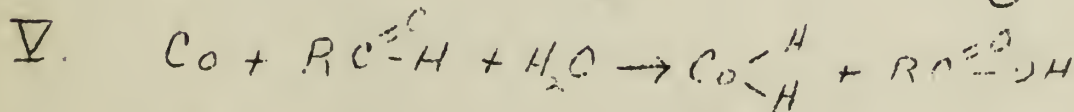
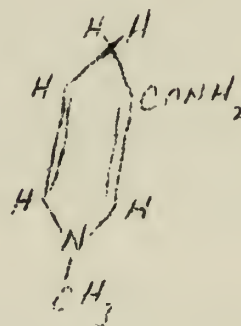
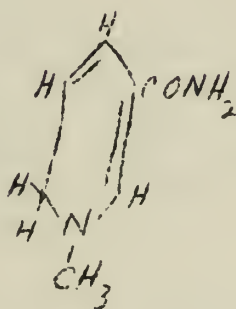
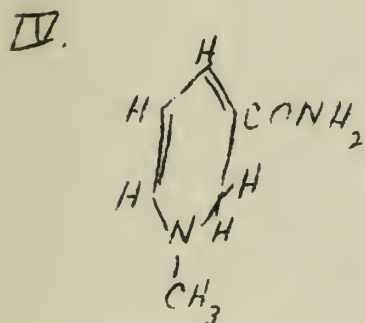
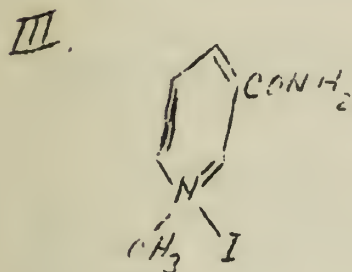
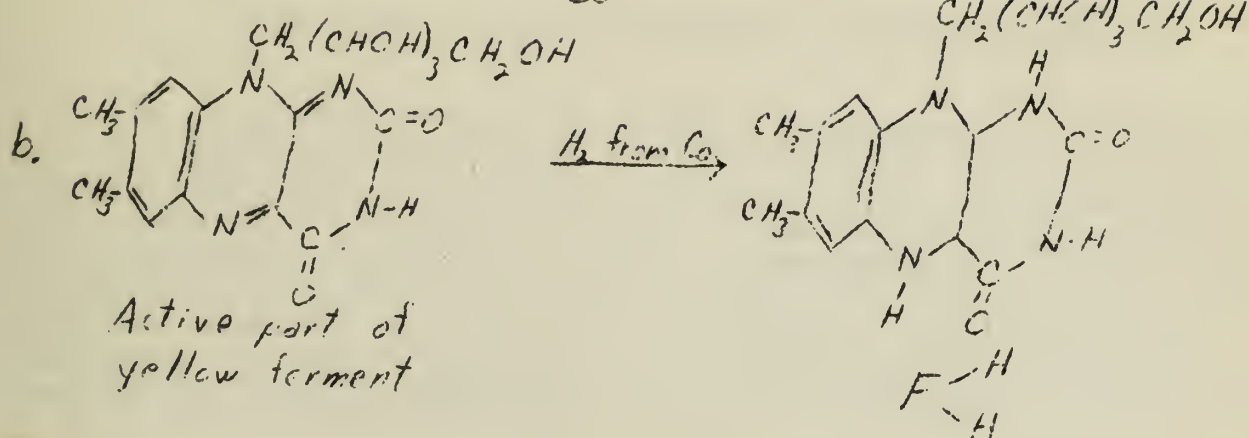
Nicotinic acid amide methyl iodide, on reduction with sodium hydrosulfite, behaves like Co. It is hydrated to a substance with spectral properties corresponding to the reduced form of Co, and is transformed by acid into a second form (inactive) with shorter wave absorption. Further, ten per cent of the para dihydro compound is formed in this reduction. From this we see that the amide is found in Co as a quaternary salt and that the reversible hydrogenation depends on this particular linkage.

From the preceding considerations, we see that vitamin B₂ has the function of an enzyme and thus there is illustrated the close connection between vitamins and ferments, which by themselves seem to be very unlike in many cases.

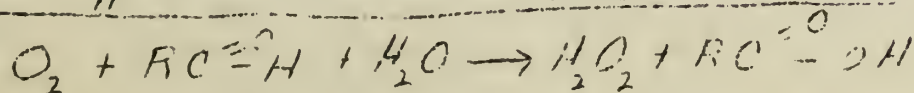


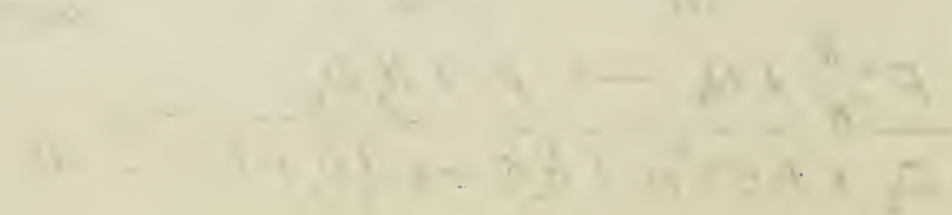
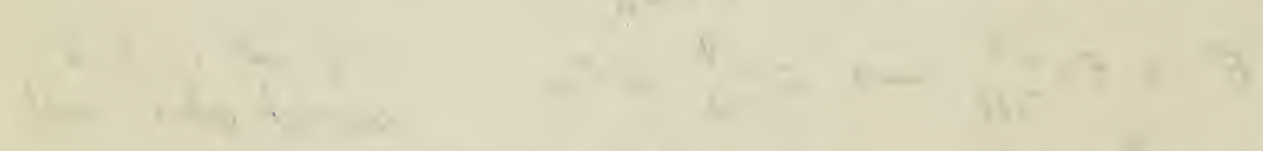
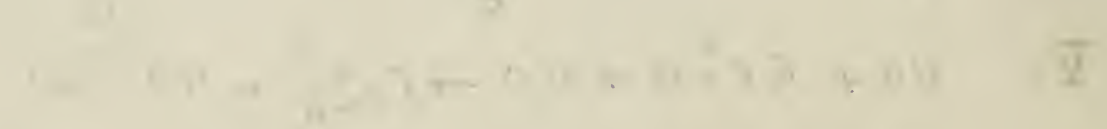
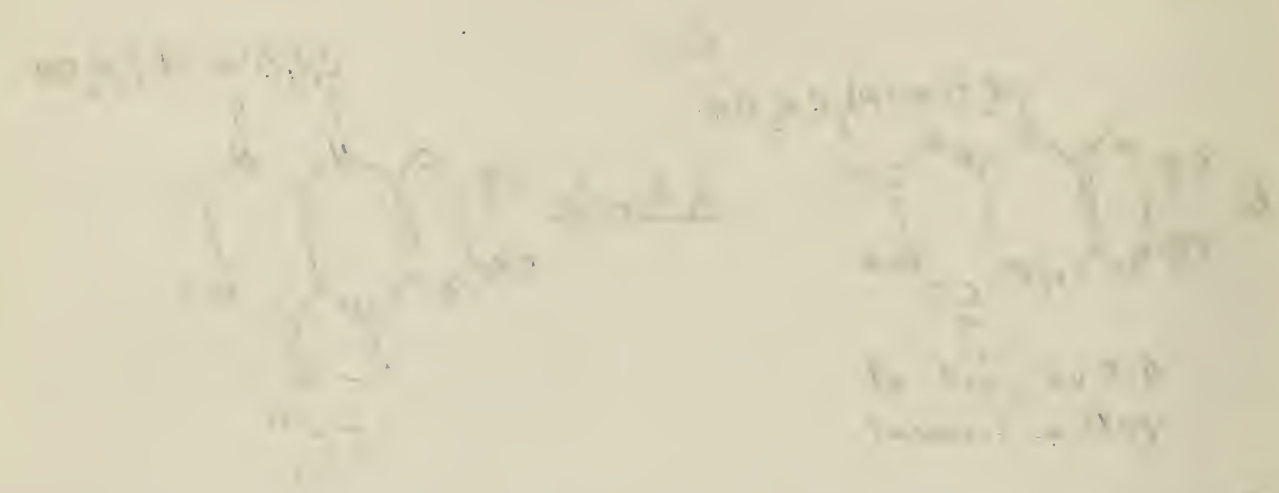


Co



$\text{RC}^{\text{O}}\text{-H}$ is hexamono-phosphoric acid.





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18, 644 (1935)
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 Wieser, "Chemistry of Natural Products Related to
 Phenanthrene," A. C. S. Monograph, No. 70.

Work done at Bayer Academy of Science, Munich.

An active poisonous principal, producing physiologically, effects upon the heart very similar to those produced by the cardiac glucosides, has been known to exist since antiquity in the secretions and skin of toads. Due to the difficulty of obtaining large enough quantities of pure material, the structures of these substances have only recently been established. The poisons exist in two series of compounds, Bufotenine and Bufotalin series. The structure of Bufotenine, $C_{12}H_{16}N_2$ (1) was established by synthesis by Wieland in 1934.

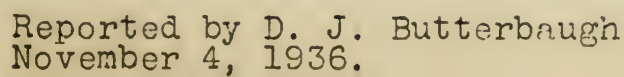
Bufotoxin, a derivative of Bufotalin, was isolated by Wieland and Alles in 1922. However, the structures of this series of compounds have remained unsolved prior to the past two years.

Bufotoxin, $C_{26}H_{37}O_6\}OCOC_{13}H_{25}O_3N_4$ (9) has been found to yield upon treatment with hydrochloric acid Bufotalin, $C_{26}H_{36}O_6$, (6) and suberyl arginine. Upon further treatment with the hydrochloric acid, Bufotalin yields Bufotalien, $C_{24}H_{30}O_{31}$, (7), one mol of acetic acid and one mol of water. A positive Liebermann-Burchard reaction indicated a sterol-like structure while its physiological action suggested a close relationship to cardiac aglucones. An unsaturated lactone ring that seems to be largely responsible for the toxic effect is known to be present. Bufotalin, upon hydrogenation, yields a product hydrobufotalin, $C_{26}H_{40}O_6$, indicating two double bonds, while a determination of active hydrogen atoms by a Grignard reagent indicates two hydroxyls, one secondary and one tertiary.

In an attempt to prove the ring system of Bufotalin, Wieland subjected acetyl Bufotalien to hydrogenation in the presence of a special catalyst from which he obtained a small yield of a crystalline acid which, upon hydrolysis, gave a substance isomeric with the known hydroxycholanolic acids but not identical. Upon pyrolytic dehydration followed by hydrogenation a product very similar to the four known cholanolic acids, but again not identical, was obtained. Wieland is inclined to believe this difference is a stereo chemical difference and not a structural difference. Bufotalin, upon treatment with selenium, yielded a small amount of a hydrocarbon identified as chrysene (8). While cinobufagin, $C_{25}H_{32}O_6$ (10), a material very similar to Bufotalin and comprising the main constituent of Chan Su was found by Tschesch and Offe to yield upon treatment with selenium at 270-350° methyl cyclopentenophenanthrene (11) thereby establishing (2) as the skeleton of the Bufotalin series.

The absorption spectra of Bufotalin indicate that the two

Placement of the hydroxyls and acetoxy group was accomplished mainly by absorption data. The tertiary hydroxyl was placed at C₁₄ by analogy to Scillaridin A, the secondary hydroxyl at C₃ by analogy to cholesterol and bile acids, while the acetoxy was placed at either C₅ or C₉. If the acetoxy were placed on C₇ a system of two more conjugated double bonds would be formed upon conversion to Bufotalien thus altering the absorption maximum. However, the absorption maximum of Bufotalin and Bufotalien were practically identical thus indicating (6) or (6a) for Bufotalin and (7) or (7a) for Bufotalien.



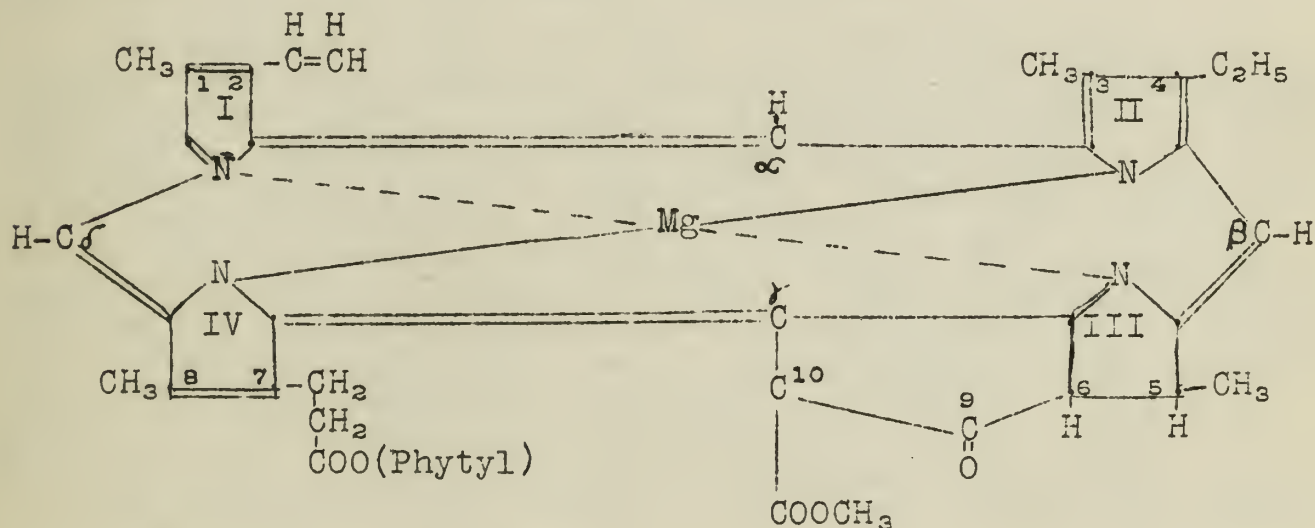
RECENT EVIDENCE ON THE STRUCTURE OF CHLOROPHYLL a

Hans Fischer,
Stern and Wenderlein,
Conant,
G. Fischer,

Technische Hochschule, Munich
" " "
Harvard University
Bayer Academy of Science,
Munich

Chlorophyll, the green pigment of plants which catalyzes photosynthesis, was isolated and correctly analyzed by Willstätter in 1906. The early work on its structure concerned the determination of the tetrapyrrole ring which is the basic nucleus of chlorophyll. The basis of this work, carried out by Willstätter and Fischer, was the drastic degradation of chlorophyll to simple pyrrole derivatives which were identified by synthesis. Fischer, using milder conditions, isolated pyrro-, rhodo-, and phylloporphyrin, (I), which contained the tetrapyrrole ring; he established the positions of the substituents in these rings by synthesis. On treating chlorophyll derivatives with HI in glacial acetic acid, Fischer isolated phylloerythrin (II), which was already recognized as an animal degradation product of chlorophyll, and whose structure Fischer fixed by synthesis. This led Fischer to propose the presence in chlorophyll a of the isocyclic carbon ring.

In 1935, Fischer proposed his present formula for chlporophyll a on the basis of the spectroscopic measurements of Stern and Wenderlein, and on chemical evidence produced by Conant and himself.



Fischer has adduced the following evidence in favor of this proposed structure. Conant had measured the basicity of the constituent pyrrole rings by potentiometric titrations, and on the basis of his results postulated the presence in chlorophyll of two pyrrole rings, one pyrrolenine ring, and one dihydro pyrrole ring. Conant's absorption spectrum data indicated that chlorins have the same relation to porphyrins as does cyclohexadiene to benzene; this indicated a dihydro porphyrin structure as basic in chlorophyll.

Stern and Wenderlein's absorption spectrum data gave strong evidence of not only the positions of the two extra hydrogens, but also of the double bond structure of the entire chlorin ring, and hence that of chlorophyll.

One of the carboxyl groups of chlorophyll is esterified with phytol, whose structure was proved in 1928 by Gottwald Fischer's synthesis; Willstätter had early shown that the other carboxyl group in chlorophyll is esterified with methanol.

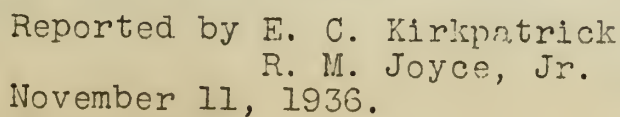
By pyrolysis of phaeophorbide a (IV) and of methyl phaeophorbide a (VI), Fischer and Conant both proved conclusively that the propionic acid group at position 7 carried the phytyl radical.

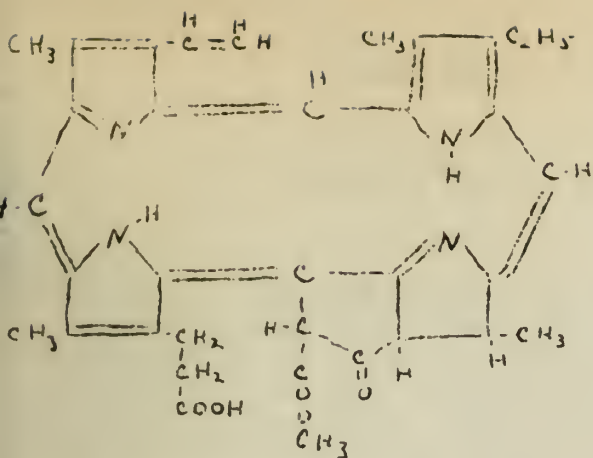
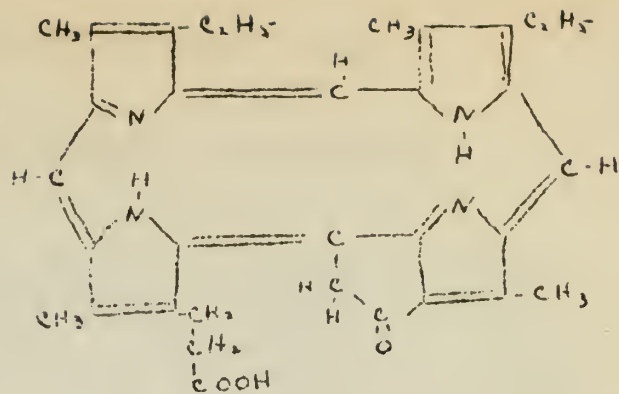
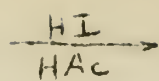
Fischer had known for some time that chlorins and phorbides, on treatment with HI in hot glacial acetic acid, yielded "oxo" derivatives. By degradation of these with HBr at 190° in a bomb acid identification of the product by synthesis, he found that the groups undergoing this "oxo" reaction was in position 2. Absorption spectrum data indicated that the "oxo" group was an acetyl group. He then proved that the acetyl group had arisen from a vinyl group by treating the chlorin with diazo acetic ester and oxidizing the product of this Buchner Curtius condensation, obtaining the acid (VIII). The structure of this acid was known since it had been obtained by a similar set of transformations from protoporphyrin, which was known to have a β vinyl group from its synthesis. Confirmation of the presence of the vinyl group was found in a study of the oxidation products of chlorophyllides and other chlorophyll derivatives.

In addition to the absorption spectrum data, Fischer has brought forth much chemical evidence for the two extra hydrogens on positions 5 and 6. A study of the optical activity of various chlorophyll degradation products demanded the presence of three asymmetric carbon atoms in chlorophyll. Since such a condition could not be fulfilled by adding hydrogens to bridge carbons nor to imino nitrogens, it was apparent that the two hydrogens appeared on one of the pyrrole rings. That no oxidation products of ring III could be isolated is best explained if these hydrogens are assigned to positions 5 and 6, since reduced alkyl pyrroles are known to be completely destroyed on oxidation. The difference in the number of active hydrogens between methyl Phaeophorbide a oxime (IX) and Phaeoporphyrin as diester oxime (X) is best explained on the basis of the nature of the bond between C₅ and C₆.

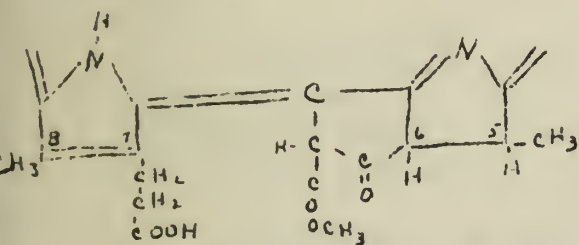
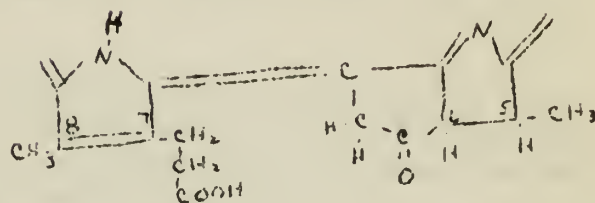
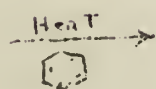
The most striking evidence in this connection is the isomerism between pseudochlorin Pe (XI) and chlorin Pe (XII). These two compounds differ only with respect to optical rotation and melting point; chlorin Pe is readily dehydrated to phaeopurpurin 18 (XIII), while pseudochlorin Pe undergoes dehydration only with difficulty, yielding, however, the same product. Hydrolysis of the phaeopurpurin 18 from either source regenerates only chlorin Pe. The

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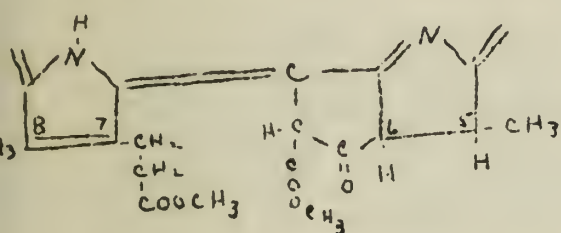
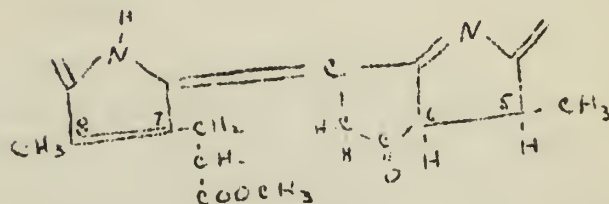
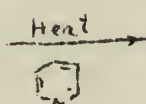


II Phaeophorbide a

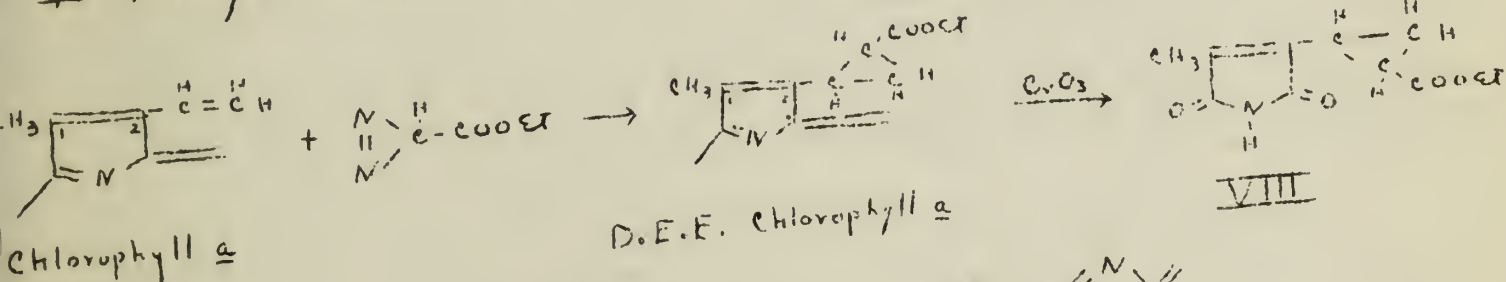
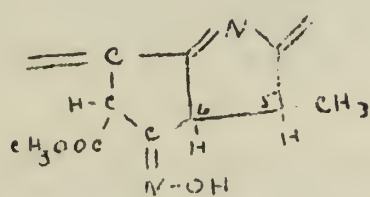
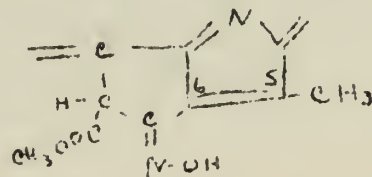
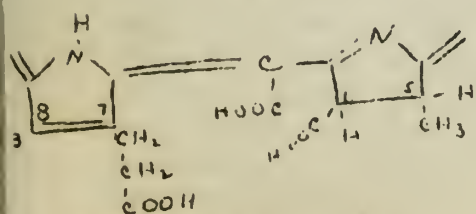
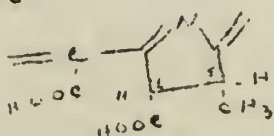
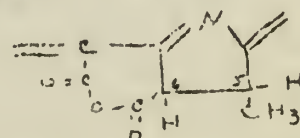
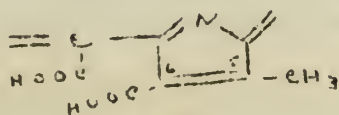
III Phylloerythrin

IV Phaeophorbide a

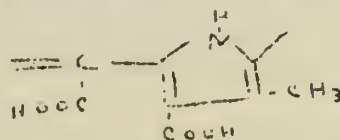
V (Methoxyl free)

VI Methyl Phaeophorbide a

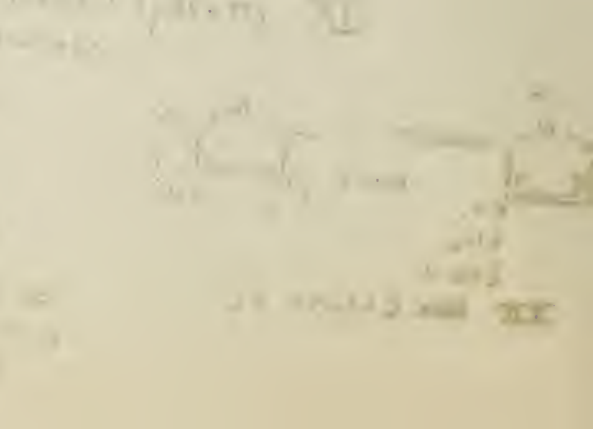
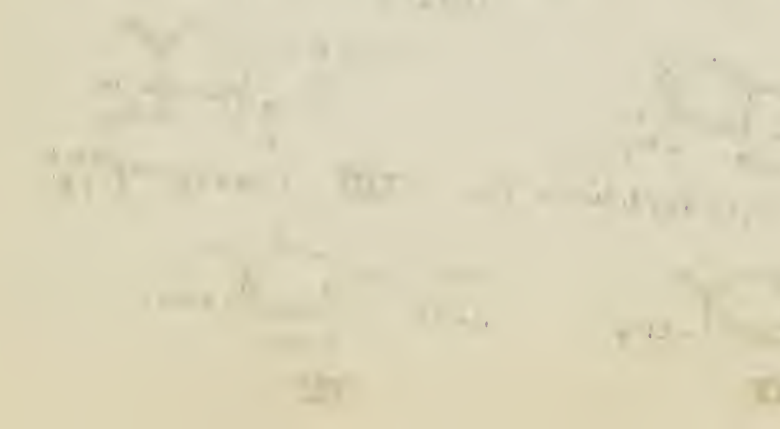
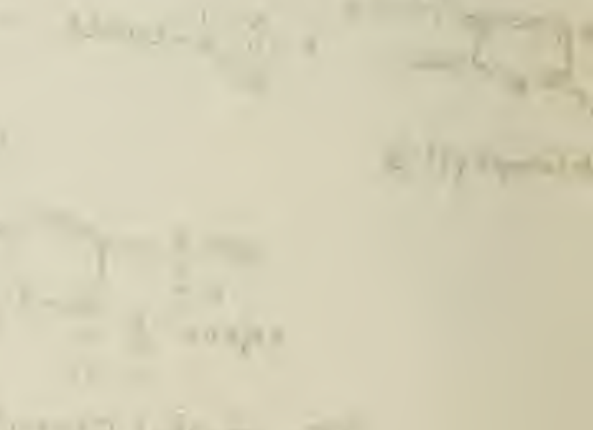
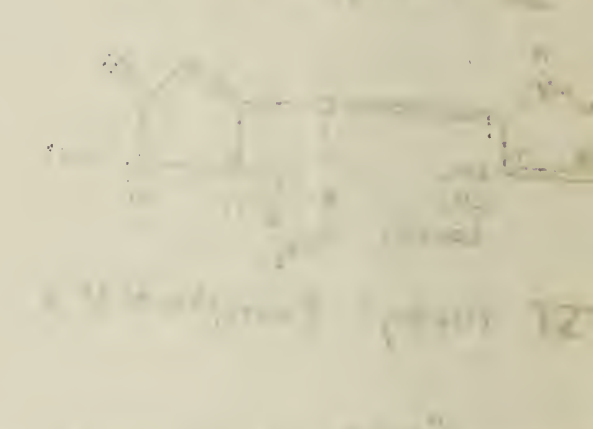
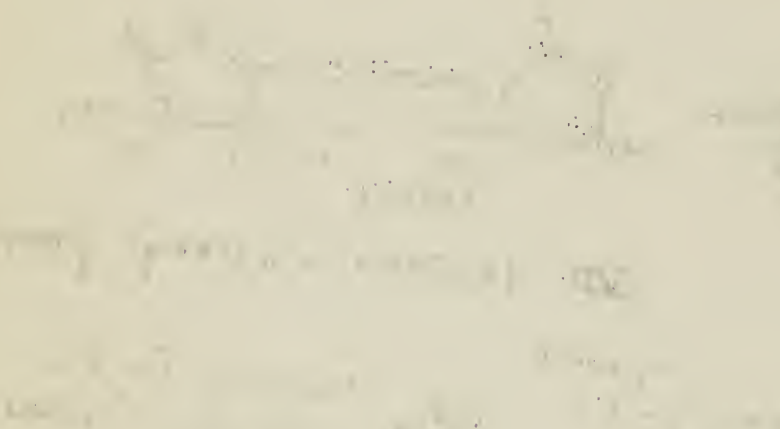
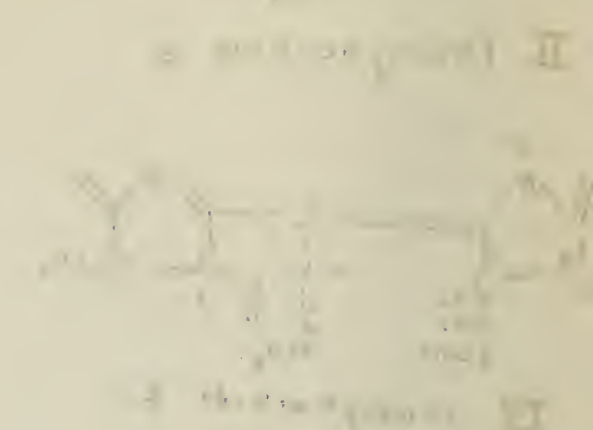
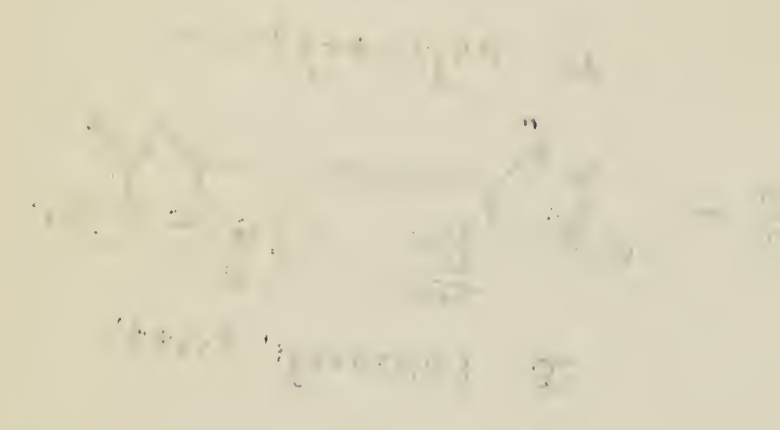
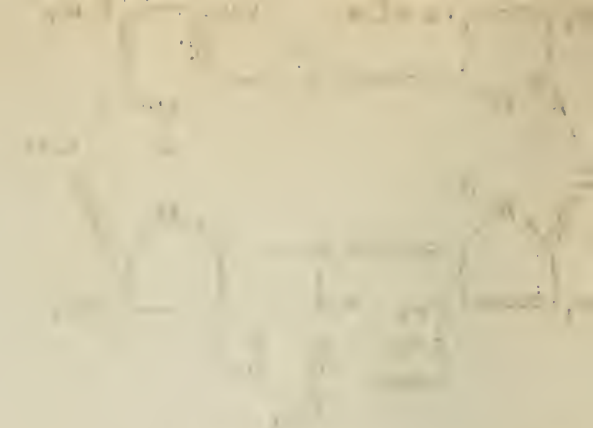
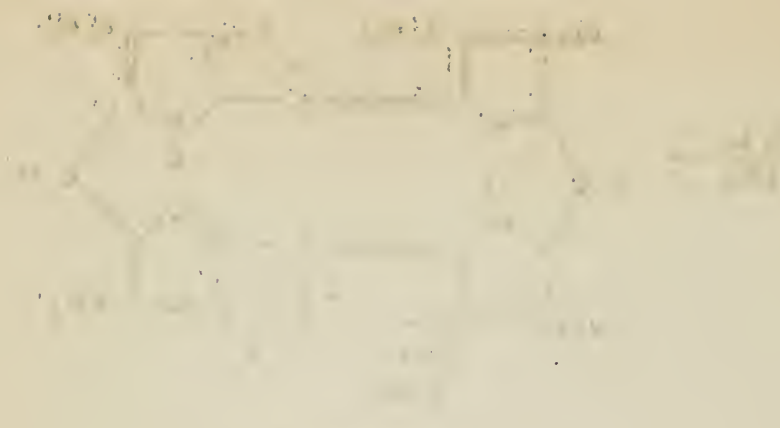
VII (Contains a methoxyl group)

Chlorophyll aD.E.E. Chlorophyll aIX Methyl Phaeophorbide a
OximeX phaeoporphyrin a5
Diester OximeXII Chlorin P6XI Pseudochlorin P6XIII Phaeopurpurin 19

XIV



XV



Richard Kuhn, Kaiser-Wilhelm Institut, Heidelberg

The synthesis of ω,ω' -di-phenyl polyenes of ~~the~~ the type $C_6H_5-(CH=CH)_n-C_6H_5$ up to the hexadecaene, where $n=8$, was reported in 1928 by Kuhn and Winterstein. These compounds, although highly unsaturated, are very stable and show no tendency to polymerize. Many cis-trans isomers may theoretically exist with these compounds, and all are known for stilbene and di-phenyl butadiene, but only one of each of the others. The regularity of melting points indicates that these are all trans forms.

The members of the series all crystallize in the same habit from a given solvent, the solubility decreasing with increasing molecular weight. The compounds are colored and are **fluorescent**, the color deepening as the molecular weight increases.

Some ω,ω' -di-biphenyl polyenes and ω -biphenyl- ω' -phenyl polyenes were also synthesized. The colors of these were more intense than in the ω,ω' -di-phenyl series.

It was found that in reducing with sodium amalgam or magnesium amalgam that the hydrogen atoms add to the terminal carbon atoms, following Thiele's rule. However, bromine addition invariably takes place 1,2, and in the long molecules the bromine atoms add on the ethylenic linkage nearest the center. This was proved by ozonation of the hexatriene which gives benzoic acid.

Highly colored molecular compounds are formed by the members of this series with trinitrobenzene and picric acid. Characteristic color reactions are exhibited with a mixture of chloroform and concentrated sulfuric acid or of chloroform, acetic anhydride, and concentrated sulfuric acid, in either chloroform or concentrated sulfuric acid solution.

Previous to Kuhn's work knowledge of the ω,ω' -polyene-dicarboxylic acids was limited to only maleic and muconic acids, in which $n=1$ and 2, respectively. The synthesis of higher members of this series seemed important, for compounds of this type have been known by stepwise decomposition of lycopin and of β -carotin.

The starting material used by Kuhn in this series of syntheses was in each case the corresponding monocarboxylic acid having two less carbon atoms. There were two general methods for obtaining these starting acids. The first consisted of condensing acetaldehyde to give aldehydes of the type $CH_3-(CH=CH)_n-CHO$ and then reacting one of these with malonic acid in pyridine solution to give an acid of the type $CH_3-(CH=CH)_{n+1}-CO_2H$. The second method, used to prepare methylated acids, consists of a Reformatsky reaction using a ketone of the type $CH_3-(CH=CH)_nCOCH_3$ and a monobromoacetic ester. The β -hydroxy acid is then dehydrated with barium hydroxide to give the conjugated polyene carboxylic acid.

Conversion of the monocarboxylic acid to the dicarboxylic is most simply illustrated by the synthesis of muconic acid **from**

crotonic. Crotonic ester (I) is converted to oxalocrotonic diethyl ester (II) by use of ethyl oxalate and potassium ethoxide in ether solution. The oxalo ester is treated with acetic anhydride, giving the O-acetyl derivative (III). The problem of replacing the acetyl group with a hydrogen has been discovered by Kuhn. Reduction with aluminum amalgam gives 1,4 addition to yield the α,α' -dihydro compound (IV). Treating this with aqueous potassium hydroxide eliminates acetic acid from the 1,4-positions, and also results in saponification, giving muconic acid (V). The overall yields are excellent.

Starting with β,β -dimethyl acrylic ester the final product is β -methyl muconic acid. Sorbic ester likewise gives 1,3,5-hexatriene-1,6-dicarboxylic acid (VI). It adds six hydrogen atoms catalytically, decolorizes permanganate, and reacts only very slowly with bromine (undiluted) to give the hexabromo acid. Sodium amalgam reduces the molecule and by 1,6 addition gives 2,4-hexadiene-1,6-dicarboxylic acid (VII), which rearranges in hot alkali to the more stable 1,3-hexadiene-1,6-dicarboxylic acid (VIII). The structure of these acids is established by absorption spectra, and by the reaction of VII with cinnamic aldehyde to give 1,12-di-phenyl-dodecahexaene.

1,3,5,7-Octatetraene-1,8-dicarboxylic acid and 1,3,5,7,9-decapentaene-1,10-dicarboxylic acid were also prepared, and are the only ones which are colored. The former is yellow with colorless alkali salts, and the latter is orange with yellow alkali salts. Both acids give a yellow solution in sulfuric acid, but the color produced by the pentaene slowly shifts through a green to a final indigo. This characteristic color change, also shown by the dimethyl ester, very closely resembles that produced by carotinoids.

The use of potassium isopropoxide was necessary to effect the condensation of ethyl oxalate with 2,4,6-octatrienoic acid. The latter may be used as the methyl, ethyl, or isopropyl ester with no effect on the yield. Ethyl oxalate would give no reaction with 2,4,6,8-decatetraenoic acid in the presence of potassium alcoholates. The use of rubidium ethoxide gave a good yield of the oxalo compound.

The solubility of the acids in this series shows a general decrease as the molecular weight increases.

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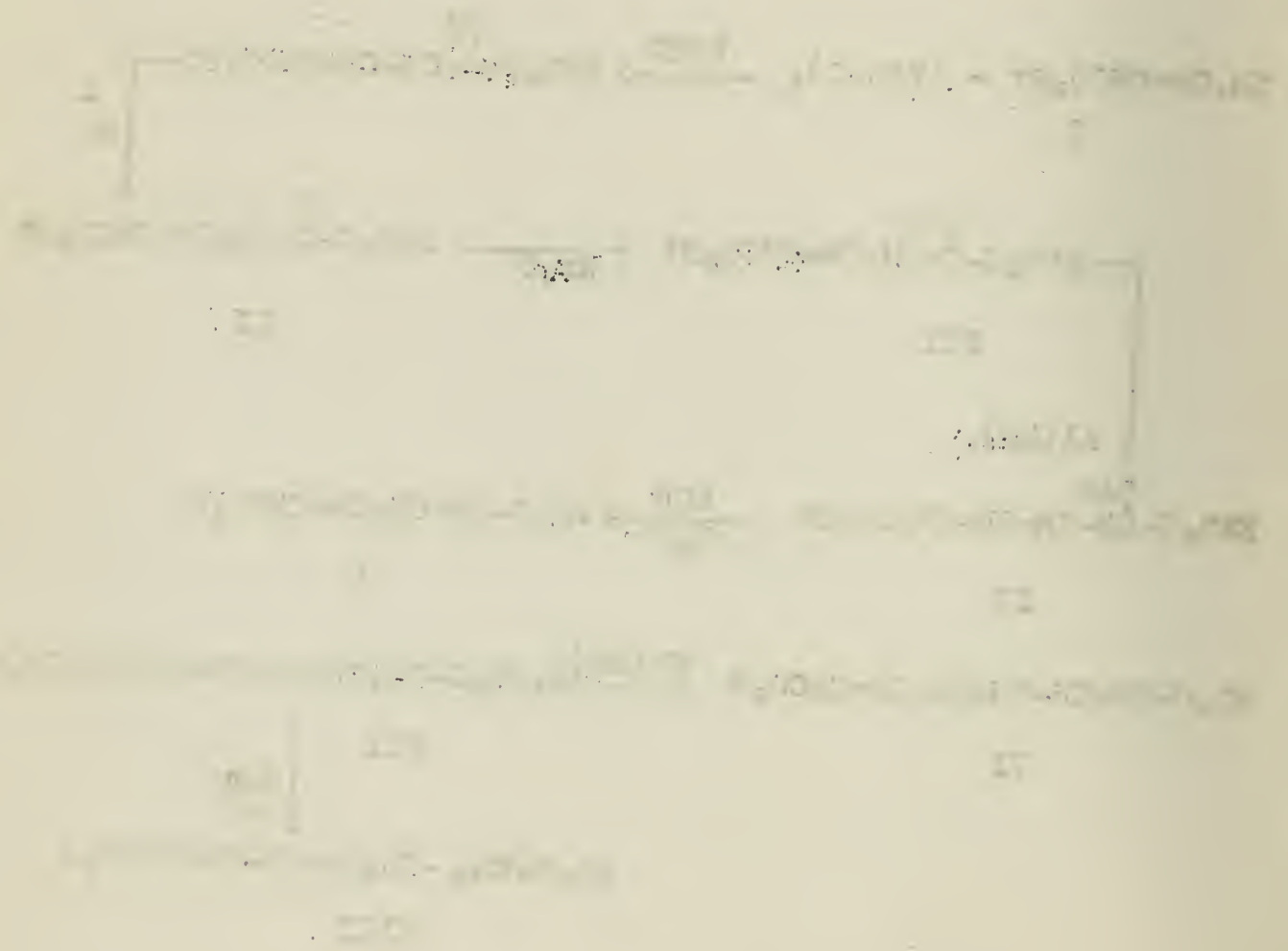
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Reported by J. H. Van Campen
November 18, 1936.

1. The first part of the paper is devoted to a general discussion of the problem.

2. The second part is devoted to a detailed study of the case of a single

3. The third part is devoted to a study of the case of a double



CANCER PRODUCING HYDROCARBONS

Cook, J. H., et al., Research Institute of the
Cancer Hospital, London.

Cancer was first described as an occupational disease by Percival Pott in 1775 when he observed the predominance of cancer in chimney sweeps. In the early part of the present century, it was noticed that workmen engaged in the distillation of coal tar were very apt to develop cancers after ten to fifteen years. Yamagiwa and Ichikawa in 1915 were the first to prove directly that the "tar cancer" arose from contact of the skin with the chemical agents present in the tars. Recently pure hydrocarbons, both synthetical and isolated from tar, have been shown to have carcinogenic properties.

Methods of testing the cancer-producing properties of a hydrocarbon include application of the substance in dilute benzene solution to the skin; subcutaneous injection of the substance in a fatty medium such as lard; and subcutaneous injection of crystals of the active hydrocarbon moistened with glycerol. Mice are the most used test animals. Cancers develop after a latent period as short as sixty days in some cases and over a year in others. Although these methods of testing are slow and laborious, no others have been entirely successful. Mayneord and Hieger made the observation in 1927 that tars and oils producing cancers had characteristic fluorescence spectra but this has not proven to be an infallible criterion for the pure hydrocarbons.

The first pure hydrocarbon shown to have carcinogenic properties was discovered in a study of a series of hydrocarbons by means of fluorescence spectra. 1,2,5,6-Dibenzanthracene (I) gave the characteristic spectral bands and was found by trial to produce cancers.

With only a few exceptions, the carcinogenic hydrocarbons known today contain a 1,2-benzanthracene ring system. Particularly active compounds are I, 1,2-benzpyrene (II), and methylcholanthrene (III). The last substance is of considerable interest since it has been prepared in the laboratory from the bile acids by reactions of a type known to occur normally in the body. While proof is entirely lacking, it may be possible that cancer may arise in the metabolic production of III or related substances from the bile acids, or perhaps from the sterols or sex hormones in the body.

Slight changes in the structure of the carcinogenic substances often have a profound effect in the activity of the compound.

Carcinogenic hydrocarbons can be prepared by the following methods; typical examples of each are given on the sheet of equations.

1. Phthalic anhydride synthesis.

The main steps in this synthesis consist of a condensation of a phthalic anhydride derivative with an aromatic hydrocarbon by the Friedel-Crafts method, followed by ring closure and reduction. Frequently, the keto acid must be reduced before cyclization in order to avoid rearrangements.

2. Pschorr synthesis.

The Pschorr method, originally developed for the synthesis of phenanthrene derivatives, consists in the condensation of an ortho nitro aldehyde with the α -carbon in a substituted acetic acid; reduction of the nitro group; diazotization; ring closure, and decarboxylation to the hydrocarbon.

3. Succinic anhydride synthesis.

Succinic anhydride is condensed with an aromatic hydrocarbon by the Friedel-Crafts method, the keto acid reduced, the ring closed, the cyclic ketone reduced and the product dehydrogenated to the aromatic hydrocarbon.

4. Elbs synthesis.

In this method, an ortho methyl diaryl ketone is heated whereby cyclization and loss of water occur at the same time giving the hydrocarbon in one step. By-products and rearrangements often occur but because of the simplicity and general applicability, this synthesis has found wide use. The example given is a slight modification of this synthesis.

5. Modified Diels-Alder reaction.

A partially reduced phthalic anhydride derivative is condensed with a substituted butadiene by the Diels-Alder reaction, the resulting anhydride decarboxylated by fusion with alkali to a mixture of hydrogenated compounds, followed by dehydrogenation to the fused aromatic system. The yields in these reactions are generally good.

Two other syntheses known as the Bardhan-Sengupta and the Perlman-Davidson-Bogert methods as applied to phenanthrene derivatives are less suitable and not so frequently applicable.

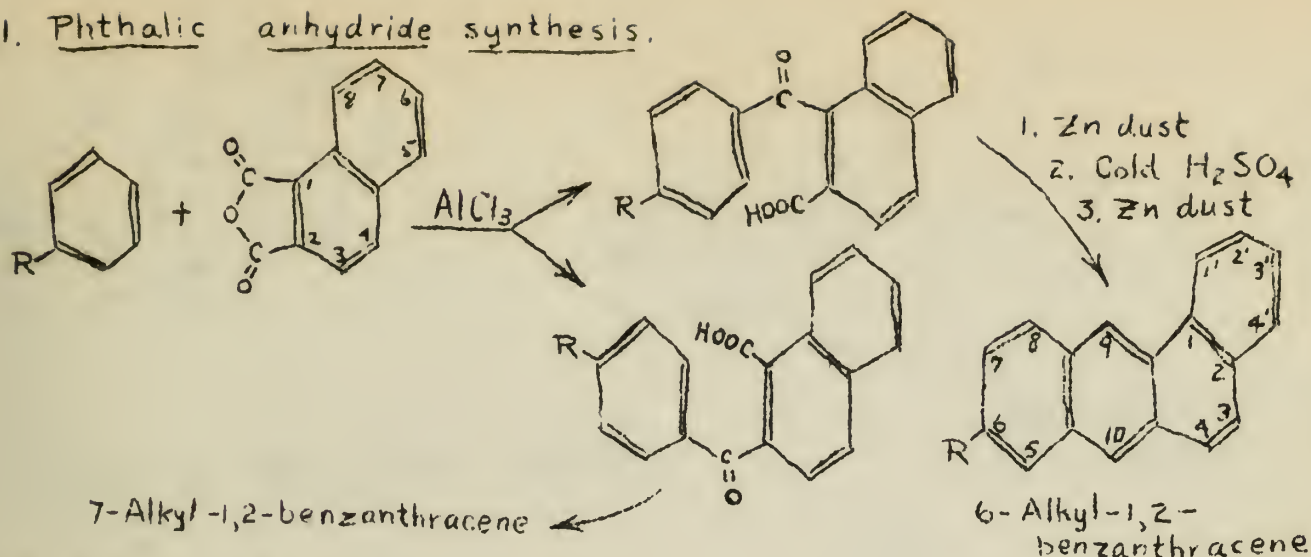
It has been postulated that there is some relation between the female sex hormone, oestrone, and cancer producing hydrocarbons. Although there is some indirect evidence that this is true, this important point has not been definitely established.

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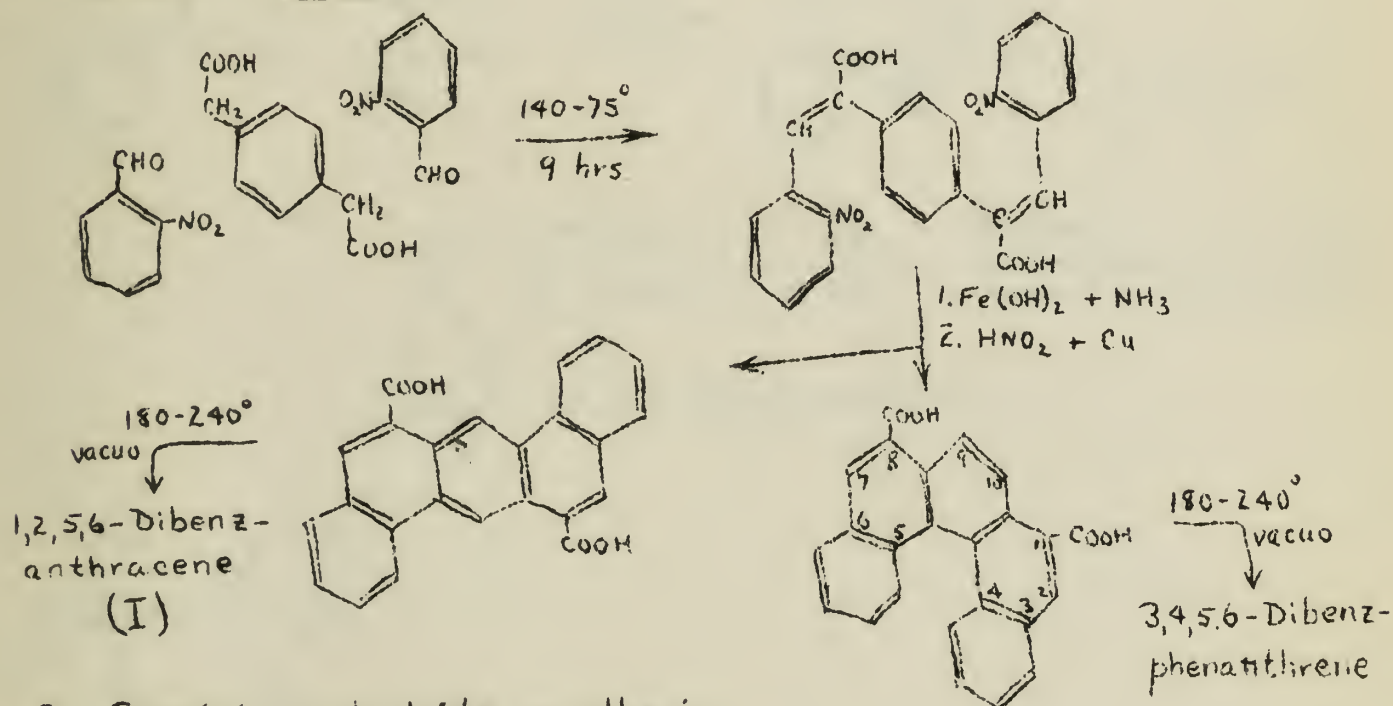
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Reported by Neil S. Moon
November 18, 1936.

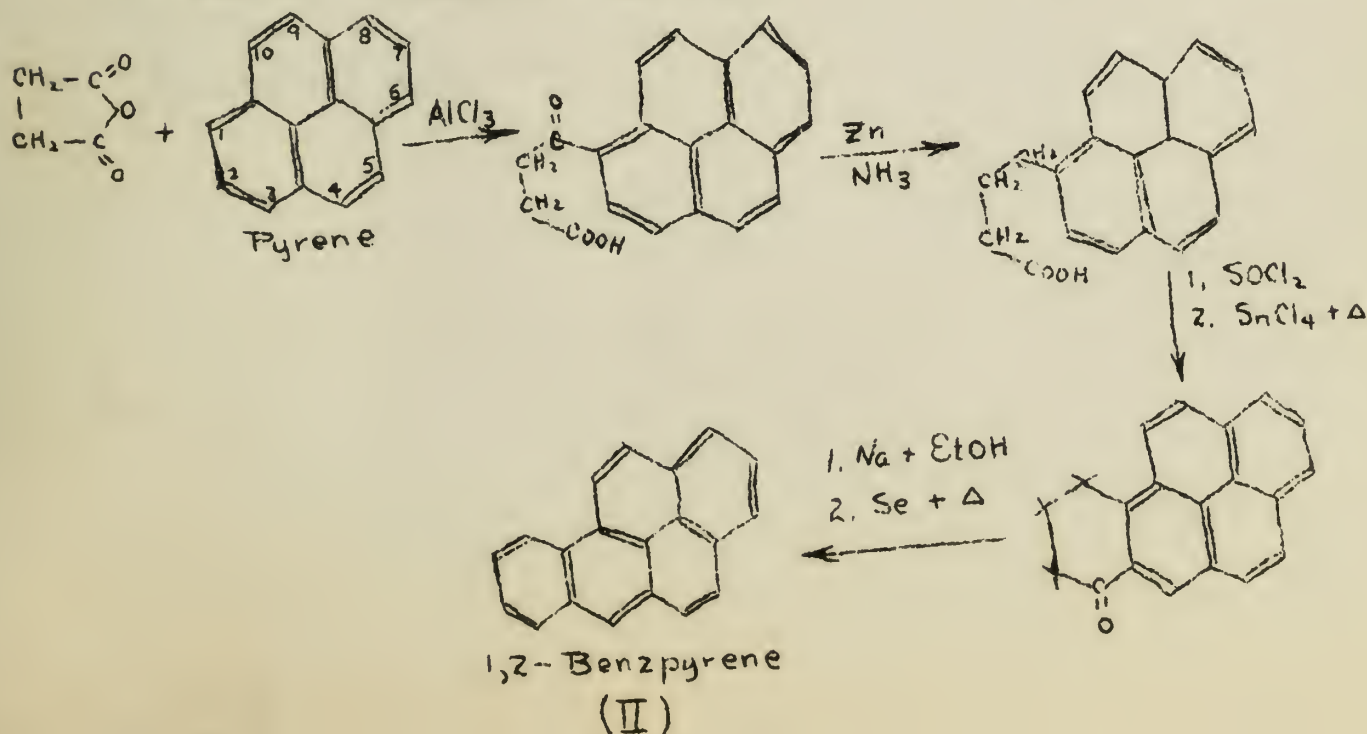
1. Phthalic anhydride synthesis.



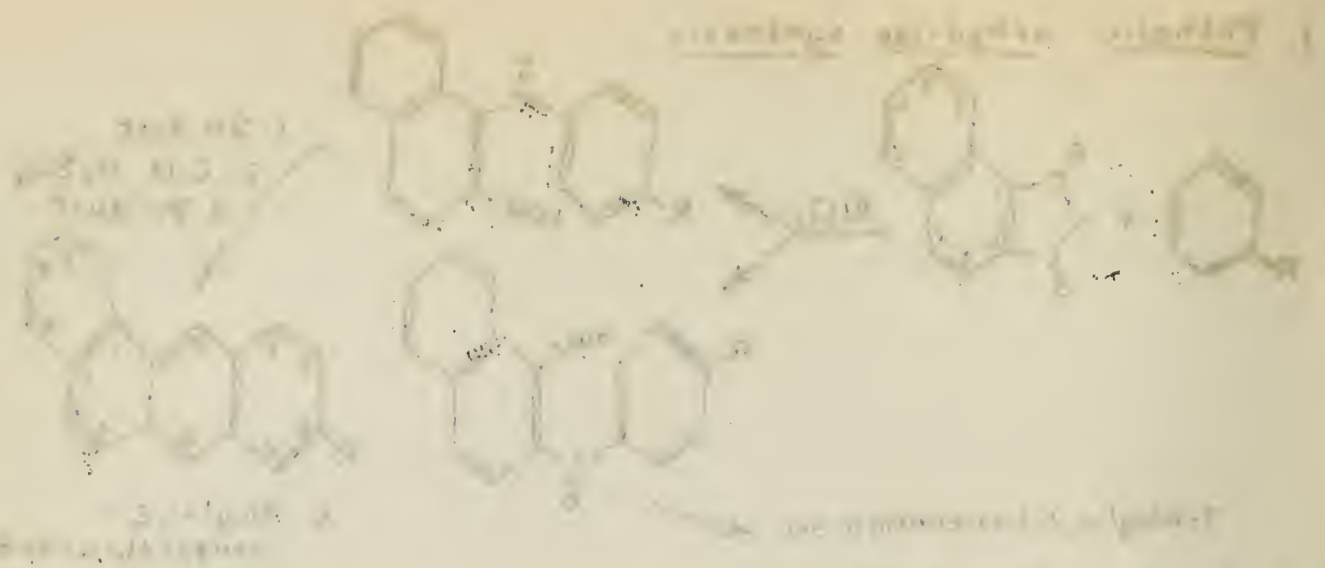
2. Pschorr Synthesis.



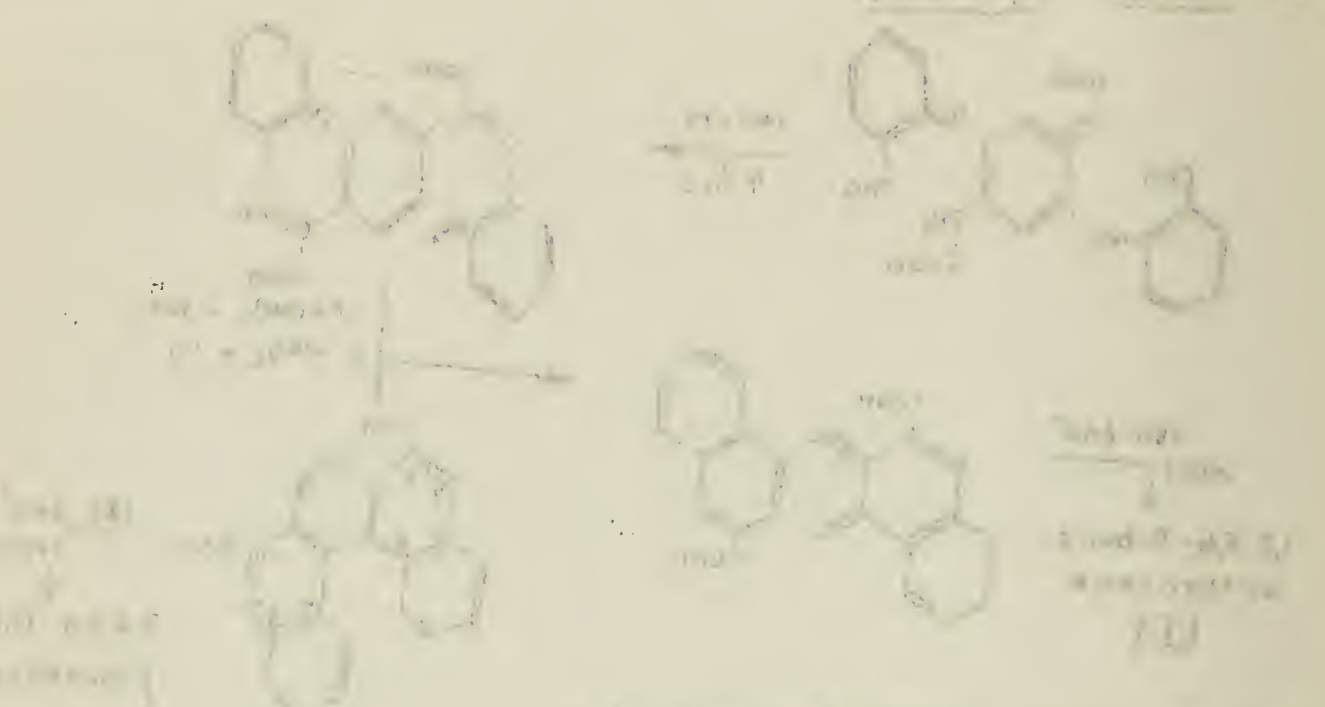
3. Succinic anhydride synthesis



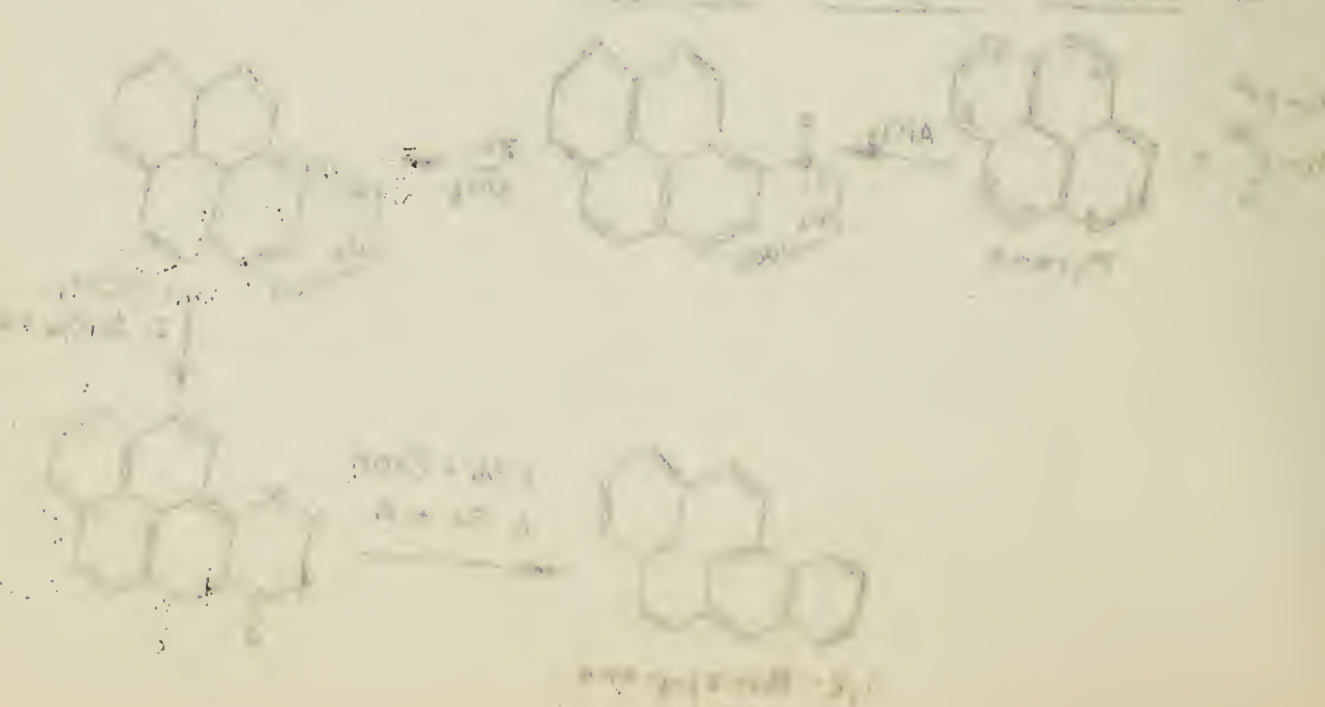
1. Polymerization of styrene

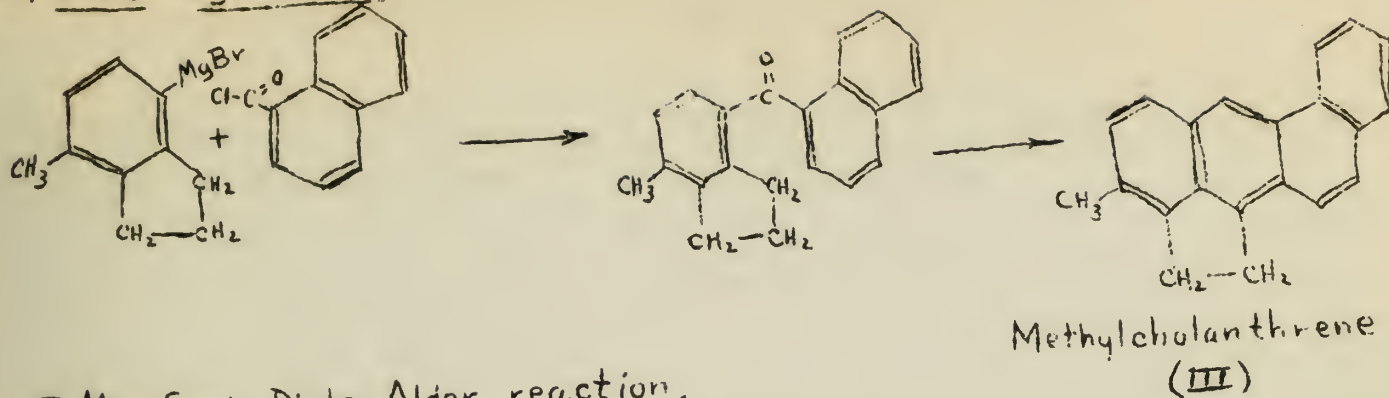
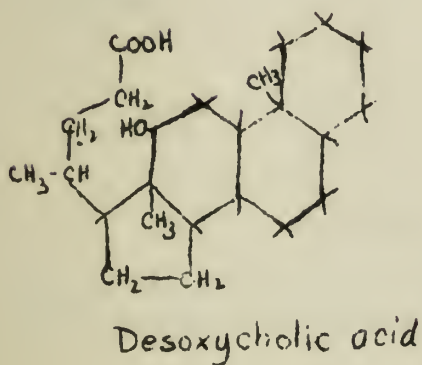
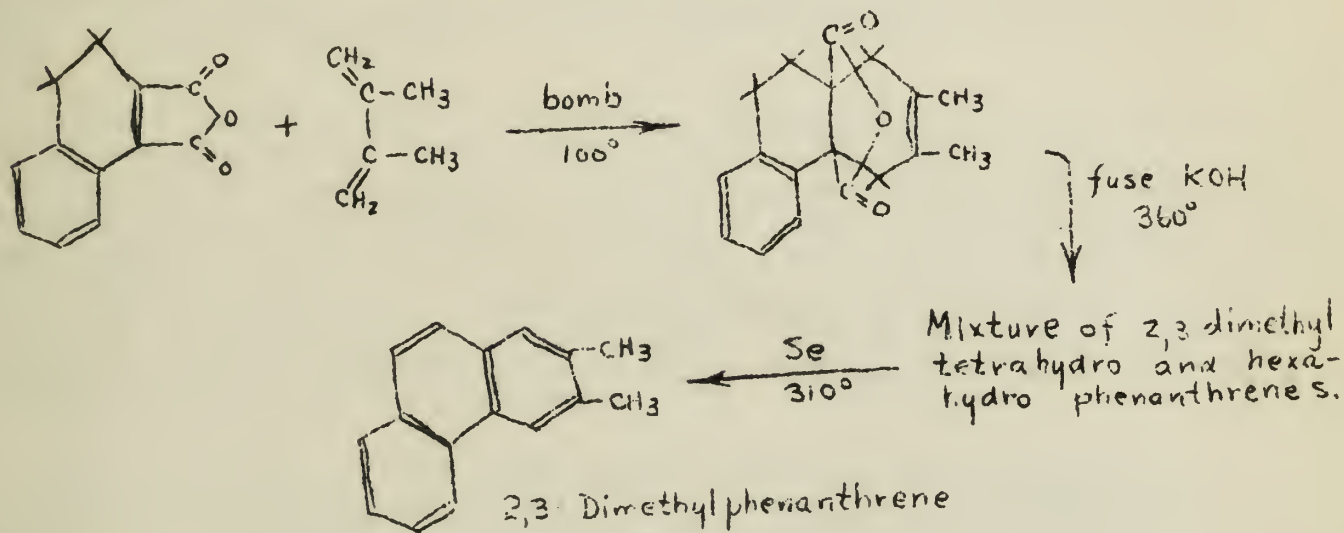


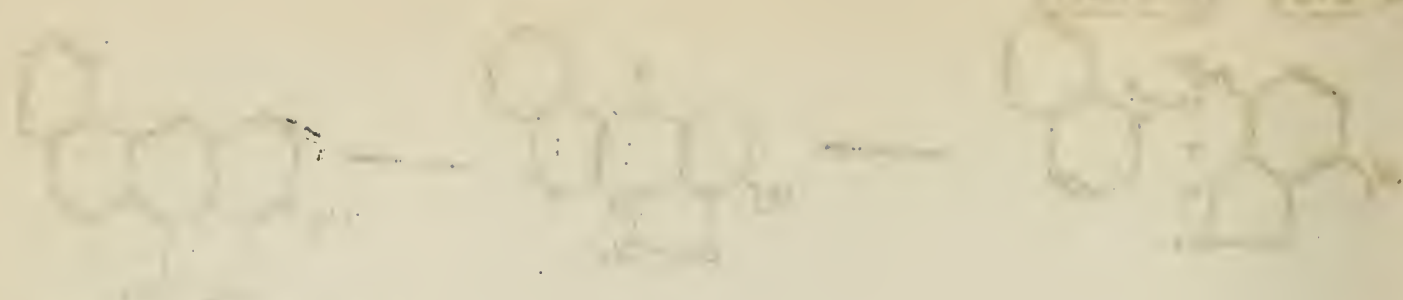
2. Polymerization of styrene



3. Polymerization of styrene

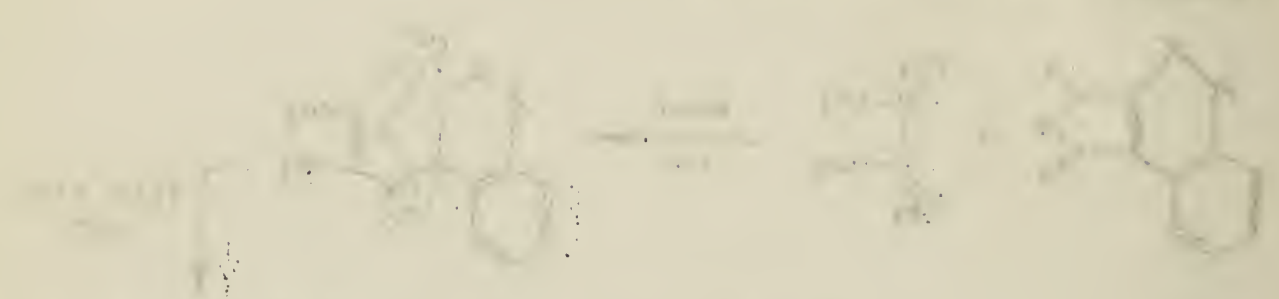


4. Elbs synthesis.5. Modified Diels-Alder reaction.

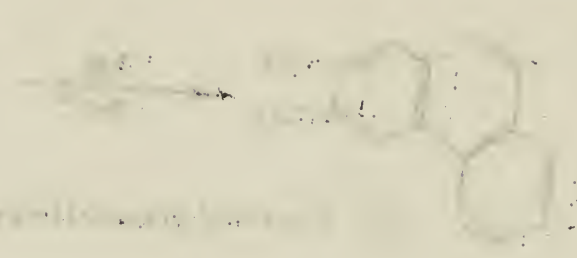


Reaction of ...

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PARAMAGNETISM AS A TEST FOR FREE RADICALS

Magnetic susceptibility, exclusive of ferromagnetism, is due to the ability of electrons, as charges moving in circuits, to act as elementary magnets, and is of two kinds. Diamagnetism is the effect of changing the velocity of the electron in the orbit by a magnetic field, and gives a small negative susceptibility which is independent of the temperature and roughly additive for the atoms and groupings present in a molecule. Paramagnetism is a large positive susceptibility varying inversely as the absolute temperature and is due to the magnetic moment of the molecule as a whole conferred by an unpaired electron, since electrons paired as in valence bonds magnetically neutralize each other in all known organic linkages.⁹

Thus, measurements of magnetic susceptibility are suitable for determination of free radicals of relatively long life. The determinations are of value, both to decide cases in argument and to furnish the theoretically important heat of free radical formation. Quantitatively, with an accuracy of ± 2 per cent of radical, the method is superior to any measurements of colligative properties of solutions of free radicals,⁶ and is surpassed only by Ziegler's more laborious methods of determining rate of reaction and extinction coefficient.

The force of orientation (F) in the field (strength H) of an electromagnet acting on a small tube (length l) of material (weight g) is determined by suspending it from the arm of a microbalance. From F the observed susceptibility ($\chi_{\text{obs.}}$) is calculated:

$$\chi_{\text{obs.}} = - \frac{2lF}{g H^2}$$

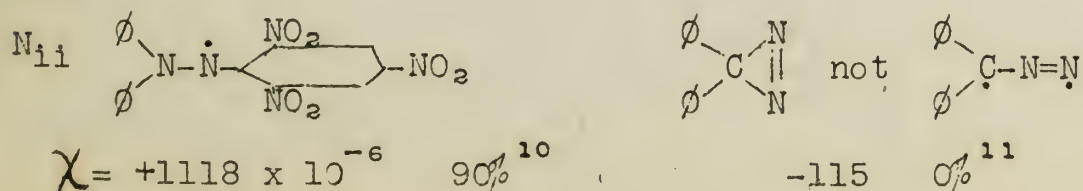
$$\chi_{\text{obs.}} \cdot M = \chi_{\text{mol}} = \chi_D + \chi_r + \chi_p$$

χ_D is the constant diamagnetism calculated from I.C.T. values for atoms and groupings.

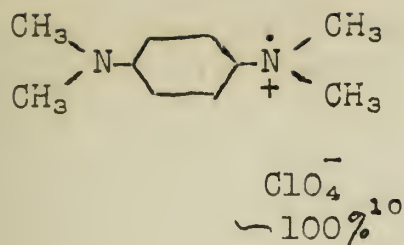
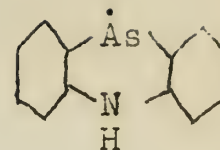
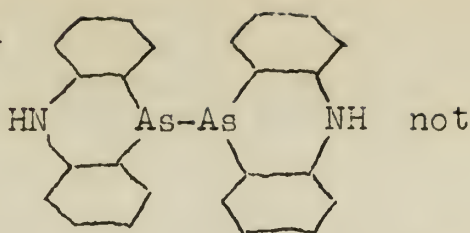
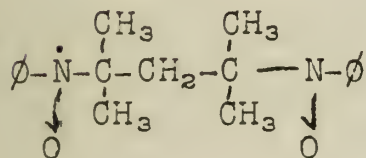
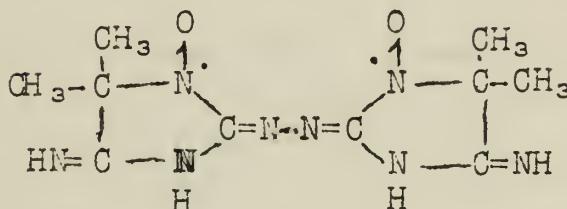
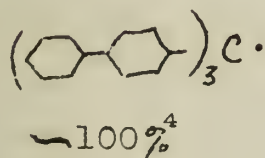
χ_r is a negligible susceptibility caused by interaction of orbits.

χ_p is the desired paramagnetism which by quantum theory should have the value $+1260 \times 10^{-6}$ e.m.u. per mol of free monoradical.^{1a}

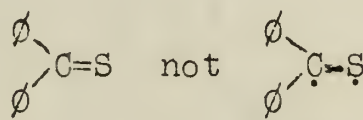
Applied to molecules loosely called free radicals, the magnetic method makes these decisions:



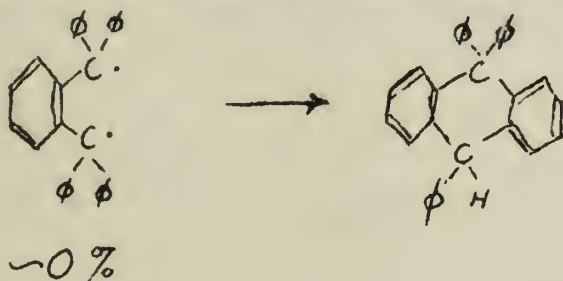
-2-

+
Ni^{III}As^{III}-215 ~0%¹⁴Ni^{IV}+1293 ~100%¹³+2080 ~80%¹³C^{III}

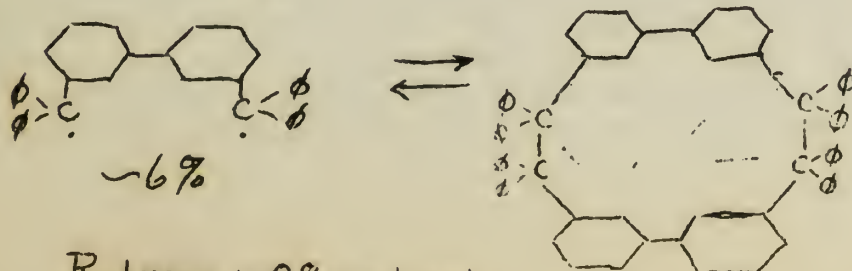
phi₃C.
agrees with
Ziegler⁶

S_I-172 ~0%¹⁴

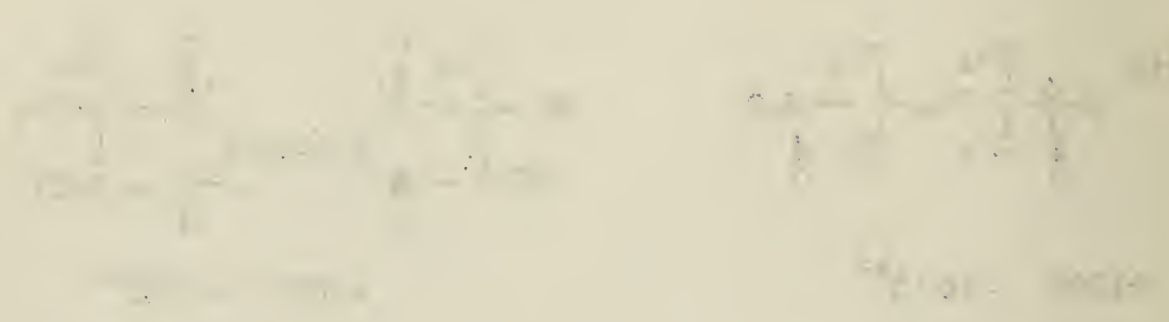
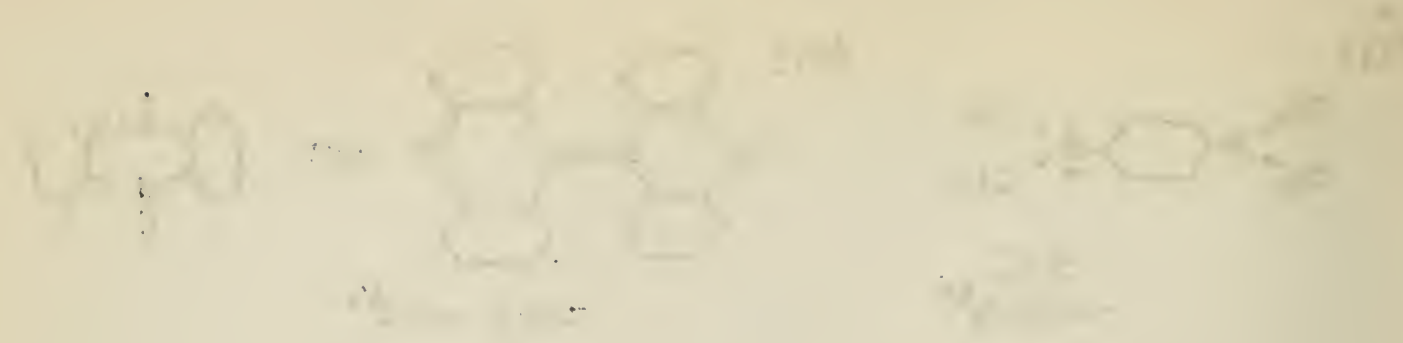
Among hydrocarbon biradicals it can be said,¹ that whenever cyclization or quinonoidation are possible, the free radical exists to the extent of less than 1 per cent.



~0%



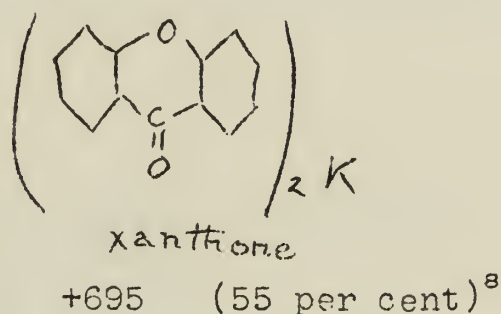
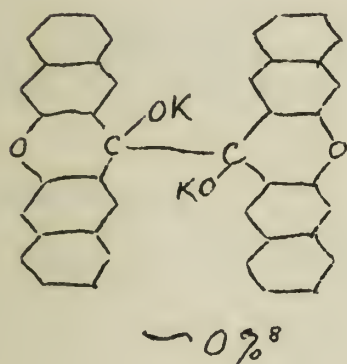
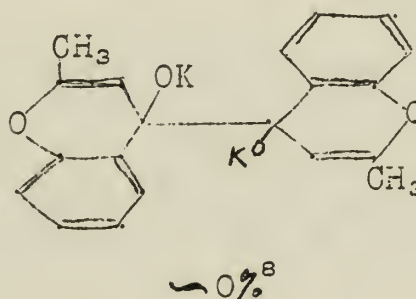
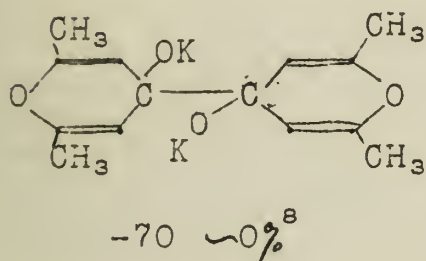
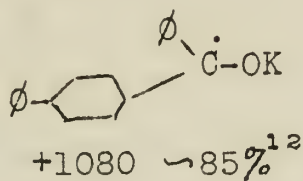
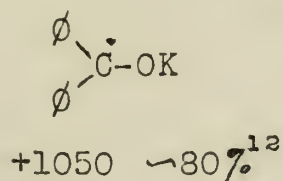
Rubrene ~0% radical



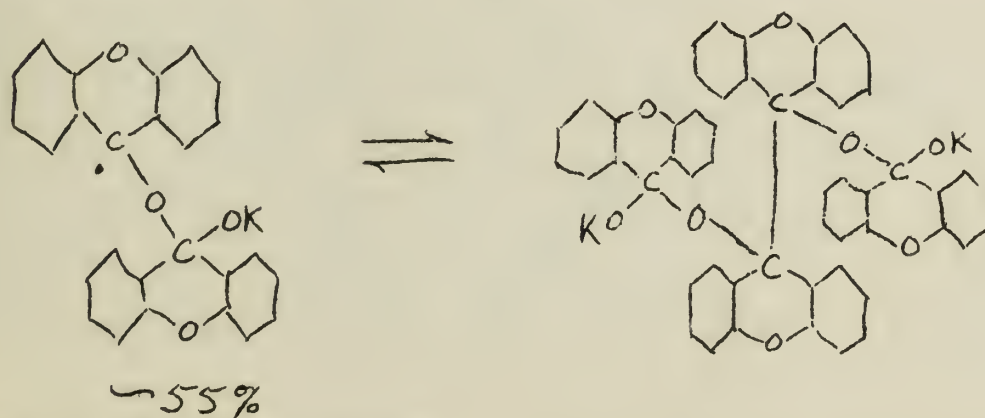
Chemical structures of 1,4-bis(phenyl)benzene and 1,4-bis(phenyl)benzene are shown. The structures are identical and represent the same molecule.



The free radical nature of Schlenk's ketyls has been recently discredited, largely by Bachmann,¹⁵ although his proof of the pinacolic structure of the compounds in acid solution may not hold for the pure substances.¹² Magnetic evidence:

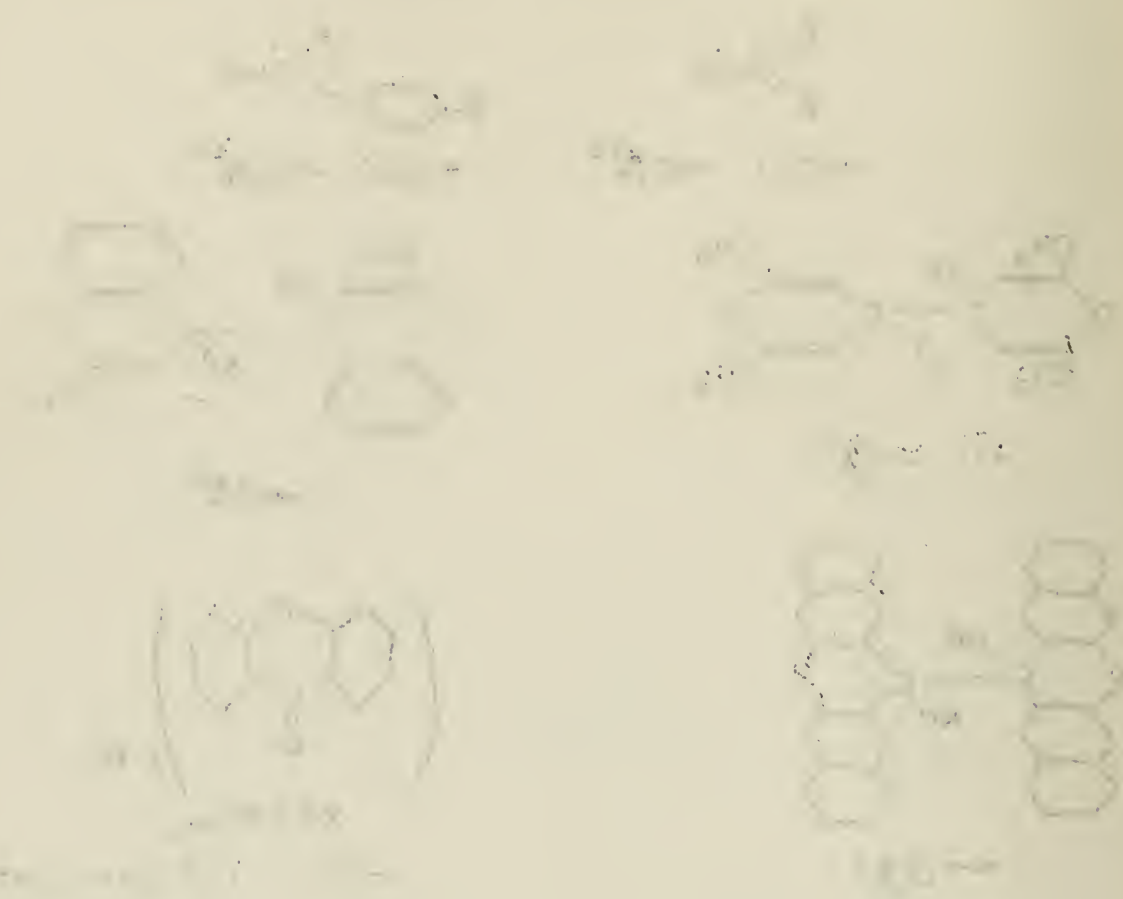


The results on xanthone indicate probable equilibrium between Schlenk's form and a Bachman form:

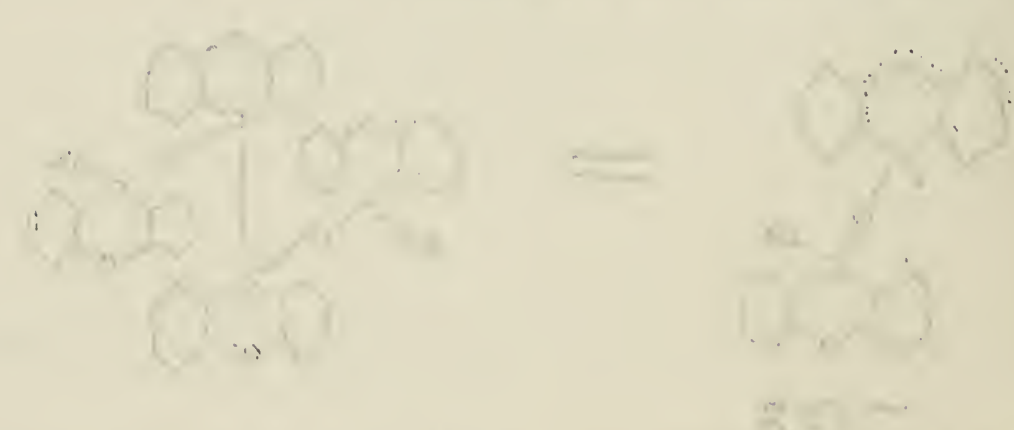


The most remarkable free radicals are perhaps those odd-molecular hydrocarbons which exhibit an unusual stability and appear not to be associated even in the solid state. To explain this and their ready electron tautomerism, Löwenbein,¹⁶ suggested "decentralization" of the free valence in this fashion:

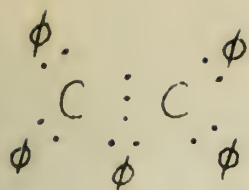
The first part of the paper is devoted to a discussion of the general properties of the system. It is shown that the system is stable and that the solution is unique. The second part of the paper is devoted to a discussion of the numerical solution of the system. It is shown that the numerical solution is stable and that the error is small.



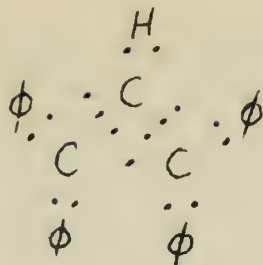
The third part of the paper is devoted to a discussion of the physical properties of the system. It is shown that the system is stable and that the solution is unique. The fourth part of the paper is devoted to a discussion of the numerical solution of the system. It is shown that the numerical solution is stable and that the error is small.



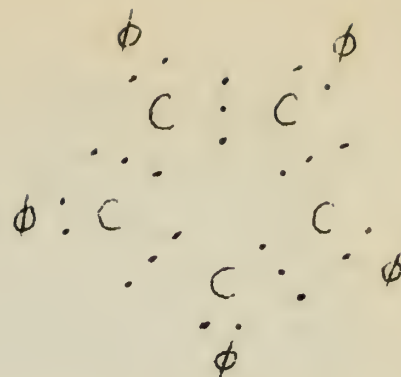
The fifth part of the paper is devoted to a discussion of the physical properties of the system. It is shown that the system is stable and that the solution is unique. The sixth part of the paper is devoted to a discussion of the numerical solution of the system. It is shown that the numerical solution is stable and that the error is small.



pentaphenylethyl



tetraphenylallyl

pentaphenyl-
cyclopentadienyl

In physical theory,¹⁷ these three-electron bonds should give paramagnetism due not only to spin moment, as with triphenylmethyl, but also due to orbital moment. The latter ought to be detected in failure of the inverse proportionality of χ with T , a thing hitherto never observed. Müller,⁷ finds that pentaphenylcyclopentadienyl gives this proportionality and no indication of orbital moment.

$\chi_{\text{mol}} = 1210 \sim 1.69$ Bohr magnetons, whereas theory gives 1.73 for simple spin moment. Thus, the concept of three electron bonds is incorrect or incomplete.

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Reported by Frank C. McGrew
November 25, 1936

The importance of trityl (triphenylmethyl) ethers derives from their use as intermediates in syntheses. They are best formed by the method developed by Helferich. Anhydroxy compound is treated with an equivalent amount of trityl chloride in anhydrous pyridine. In general, only phenolic and primary alkyl hydroxyls react. These ethers are quite stable toward water or alkali, but are easily hydrolyzed by dilute mineral acid. This property is the basis of a smooth method for forming ethers and esters containing free primary hydroxyls. Helferich's synthesis of β -glyceryl benzoate (I) illustrates this.

This method has been used by several workers to synthesize sugars and sugar derivatives. In determining the structure of the disaccharide vicianose, Helferich first prepared 6-trityl- α -glucose (II), treated this compound with acetic anhydride and separated the resulting 1,2,3,4-tetra-acetyl-6-trityl- β - α -glucose (III) from the α isomer. The trityl group was removed by dilute acid hydrolysis and the resulting 6-hydroxy compound (IV) coupled with acetobromo- α -arabinose. Hydrolysis of the acetylated disaccharide obtained (V) by the Zemplen method gave 6- β - α -arabinosido- α -glucose (VI), which was identical with naturally-occurring vicianose.

By similar methods, the structure of the following disaccharides were established: Melibiose--6- β - α -galactosido- α -glucose; cellobiose--4- β - α -glucosido- α -glucose; gentiobiose--6- β - α -glucosido- α -glucose; primverose--6- β - α -xylosido- α -glucose. Helferich has extended the method to the synthesis of tri- and tetrasaccharides and of α and β glycosides and their derivatives. By the use of the latter, he showed that the activity of Hefe's ferment for α - α -glucosides closely paralleled the specific activity of emulsin for β - α -glucosides. He has also used the trityl ethers in the synthesis of unsaturated sugars similar to VII, and in studying the problem of acyl wandering in sugars.

Trityl ethers offer a promising method of attack on the question of the equilibrium of the "oxo" and cyclic forms of sugars, and the relative activities of the two forms in physiological processes. Stepanow and Stepanenko reasoned that in 6-trityl glucose the introduction of the heavy negative trityl radical next to the carbon carrying the oxygen bridge should favor the predominance of the "oxo" form. Comparing the rates of addition of HCN to glucose and to 6-trityl glucose, they found the latter to be 29 per cent more reactive, indicating an increase in the equilibrium amounts of "oxo" form.

Trityl ethers of phenols undergo rearrangements on heating, the trityl radical migrating to the aromatic nucleus, preferably to the para position. Van Alphen, Schorigin, and Boyd and Hardy showed the reaction to be general for many phenols. When the para position is already occupied, the ethers are prone to decompose to form dyes on heating, although small yields of α -trityl phenols may be obtained. An exception to this rule has recently been reported by Funakubo and Hirotsani. They found that the trityl ether of iso-engenol (VIII) rearranged to give

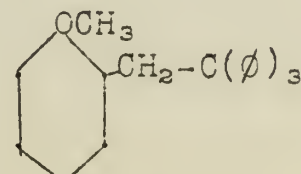
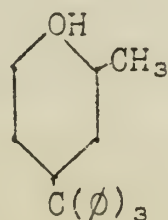
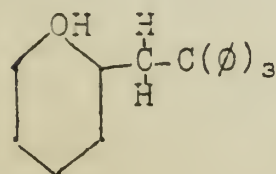
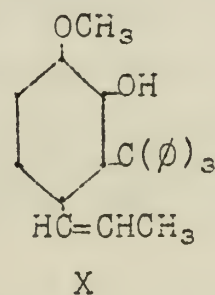
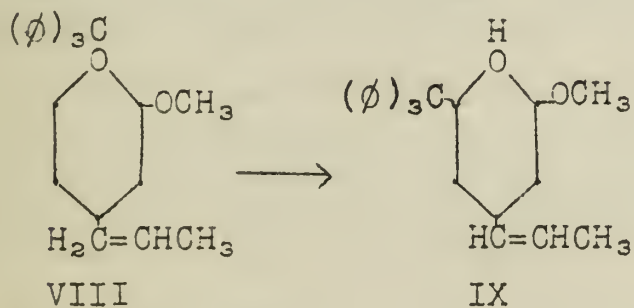
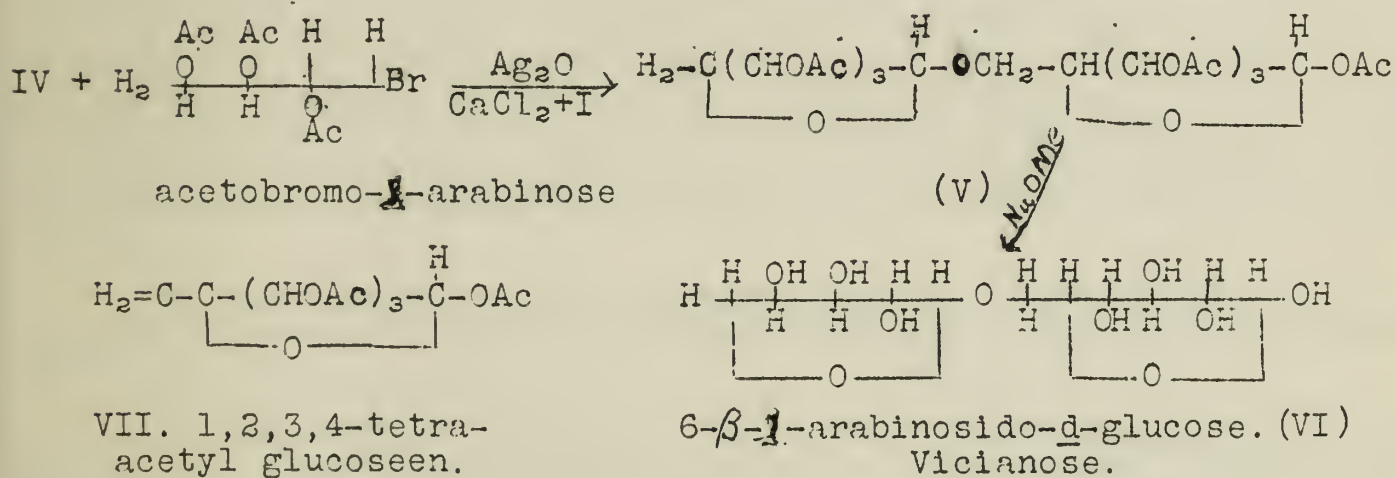
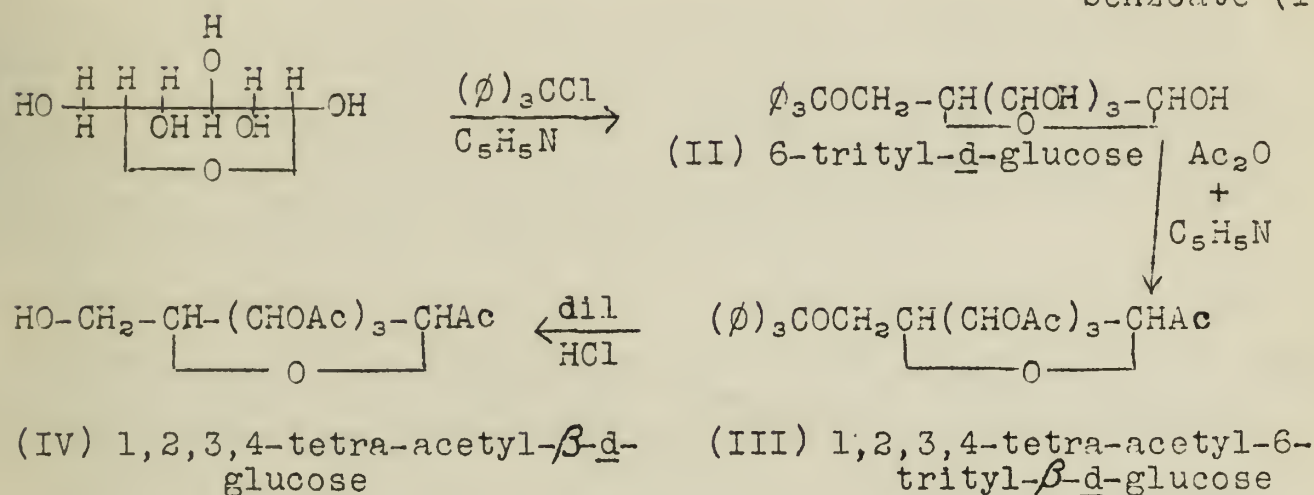
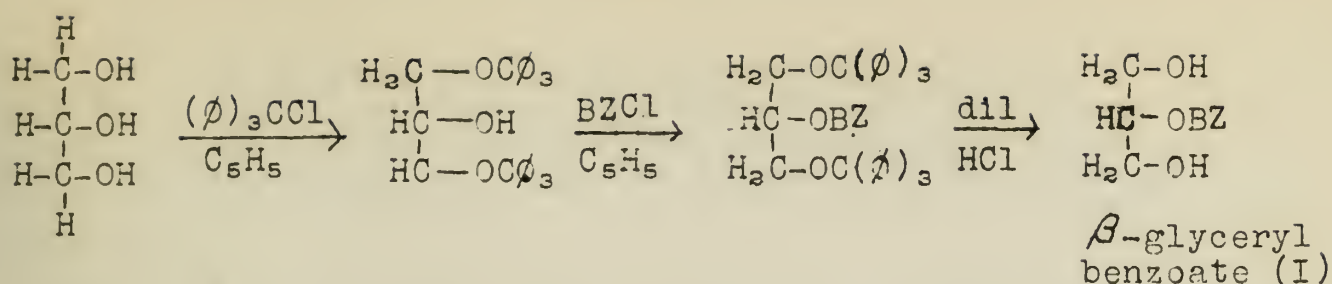
good yields of the o-trityl phenol (IX). They also claim to have obtained (X) from the trityl ether of iso-chavibetol, but the evidence reported for its structure is not conclusive.

Schorigin and Van Alphen reported an unusual rearrangement in this series. On heating the trityl ether of o-cresol, they obtained a phenol to which they assigned the structure XI. The evidence in support of this mechanism comprised the isolation of triphenyl carbinol as an oxidation product and triphenyl methane as a reduction product. Later Boyd and Hardy showed that this behavior on oxidation and reduction was also characteristic of p-trityl phenol and p-trityl-m-cresol. They concluded that Schorigin's product was actually p-trityl-o-cresol (XII). However, four years later Porter and Parsons synthesized o-2-methoxyphenyl- β,β,β -triphenylethane (XIII). They found this to be identical with the methylation product of Schorigin's phenol.

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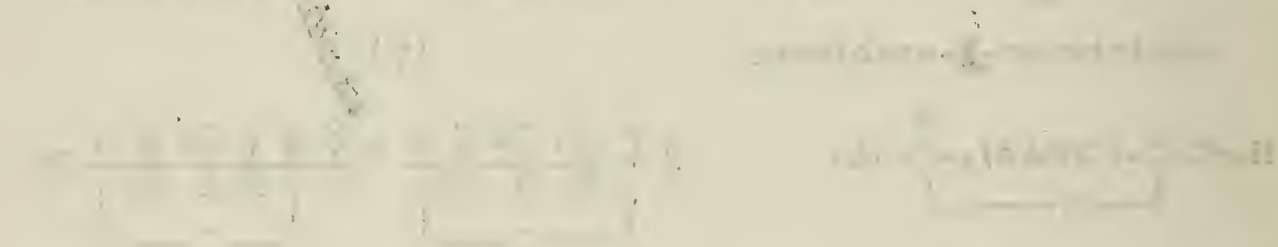
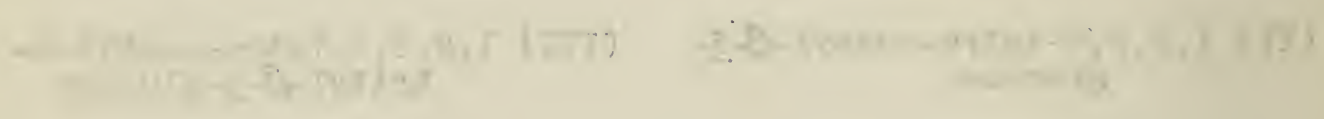
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Reported by C. L. Levesque
November 25, 1936.





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NEW REAGENTS FOR ALDEHYDES AND KETONES

Girard and Sandulesco, University of Paris
Borek and Clarke, Columbia University
Anchel and Schoenheimer, Columbia University
Galloway and Read, The University, St. Andrews

In the last few years there has been a voluminous amount of research upon the isolation of sexual hormones. This research has produced several new reagents which are of considerable use in the isolation of these ketones. The more important of these reagents are I pcarboxyphenylhydrazine, II carboxymethoxylamine, III trimethyl acethydrazide quaternary ammonium chloride (Reagent T), and IV acethydrazide pyridinum chloride (Reagent P).

These reagents are prepared as indicated on the last page.

Anchel and Schoenheimer have found that I and II can be used to isolate the total ketone fraction from natural material and to separate alpha-beta unsaturated ketones from the saturated ketones.

Reagent II is better for separating total ketone fractions. The compound formed by action of II upon ketones is soluble in K_2CO_3 (dil.) and insoluble in ether. Reagent I is better for separating alpha-beta unsaturated ketones from saturated ketones. This separation is based upon the ease of hydrolysis of the hydrazones. 37% formaldehyde in 95% ethyl alcohol hydrolyzes the saturated hydrazones but not the unsaturated hydrazones. The latter may be separated from the saturated ketones and subsequently hydrolyzed by pyruvic acid in 95% alcohol.

The hydrazones of I are autooxidizable; hence, they must be used in absence of air. The oximes of II are stable in the presence of air.

Girard and Sandelesco have found that reagents III and IV may be used to isolate total ketone fractions from complex natural material and to separate ketones and aldehydes. IV may be used as a microchemical characterization of the carbonyl group.

Reagent III is highly deliquescent, reagent IV is not.

To separate total ketone fractions from natural material the hydrazones are formed. The aqueous solution is extracted with ether to remove the other natural material, and yields upon subsequent acidification the free ketones.

The hydrazones of both these reagents are most stable at pH values of 6.5 to 7.0. At lower values the ketonic hydrazones are readily hydrolyzed. The hydrazones of aldehydes are very stable to hydrolysis, affording a method of separation of aldehydes and ketones.

Iodomercuric solution is used for a qualitative determination of the carbonyl group. It is added to the aqueous solution of the hydrazone of reagent IV. A turbidity is produced if carbonyl is present. The reagent for this test must, of course, be especially purified.

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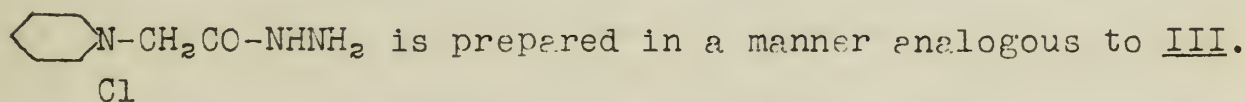
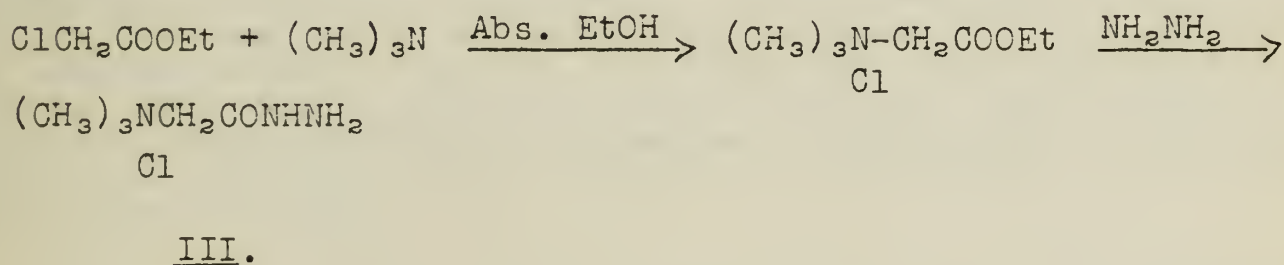
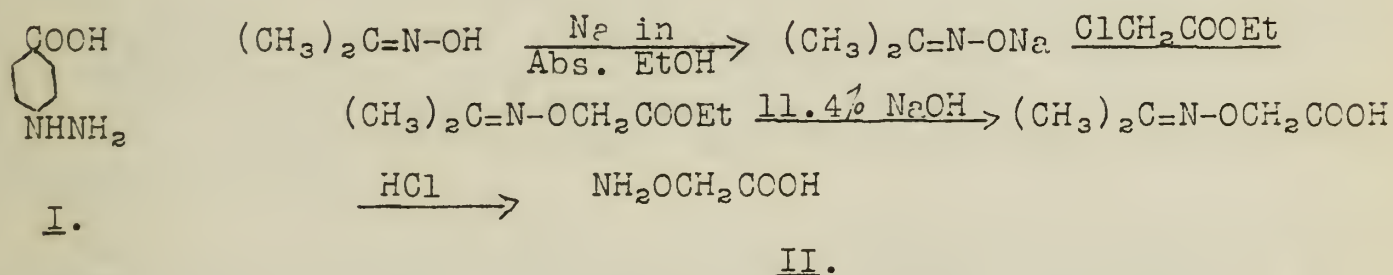
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These reagents are not used for identification of these substances so much as for isolation from the natural material.

Galloway and Read have found that d-neomenthyl glycinehydrazide, $C_{10}H_{19}NHCH_2CO-NH-NH_2$, is a potential resolving agent of great promise for optically active aldehydes and ketones. The hydrazones are easily hydrolyzed by shaking in ethereal solution with dilute mineral acids.

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IV.

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INTO THEIR NEXT HIGHER HOMOLOGS OR THEIR DERIVATIVES

F. Arndt--formerly of the University of
Breslau, now of Istanbul, Turkey
B. Eistert--I. G. Farbenindustrie A. G.

In 1915 Nierenstein and Clibbens reported that ω -chloroketones could be formed by the action of diazomethane on some aromatic acyl chlorides.

Arndt, Eistert and Partale in 1927, and Bradley and Robinson in 1928 failed at the preparation of certain ω -chloroketones by this method, and instead obtained ω -diazoketones.

Arndt and Amende found the discrepancy due to the manner in which the reactants were combined. If the diazomethane is added to the acyl chloride an ω -chloroketone is formed. If the process is reversed, an ω -diazoketone is formed.

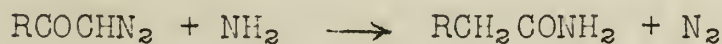
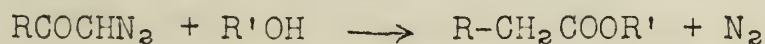
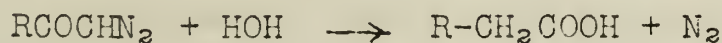
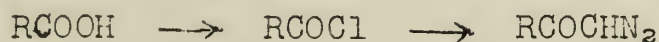
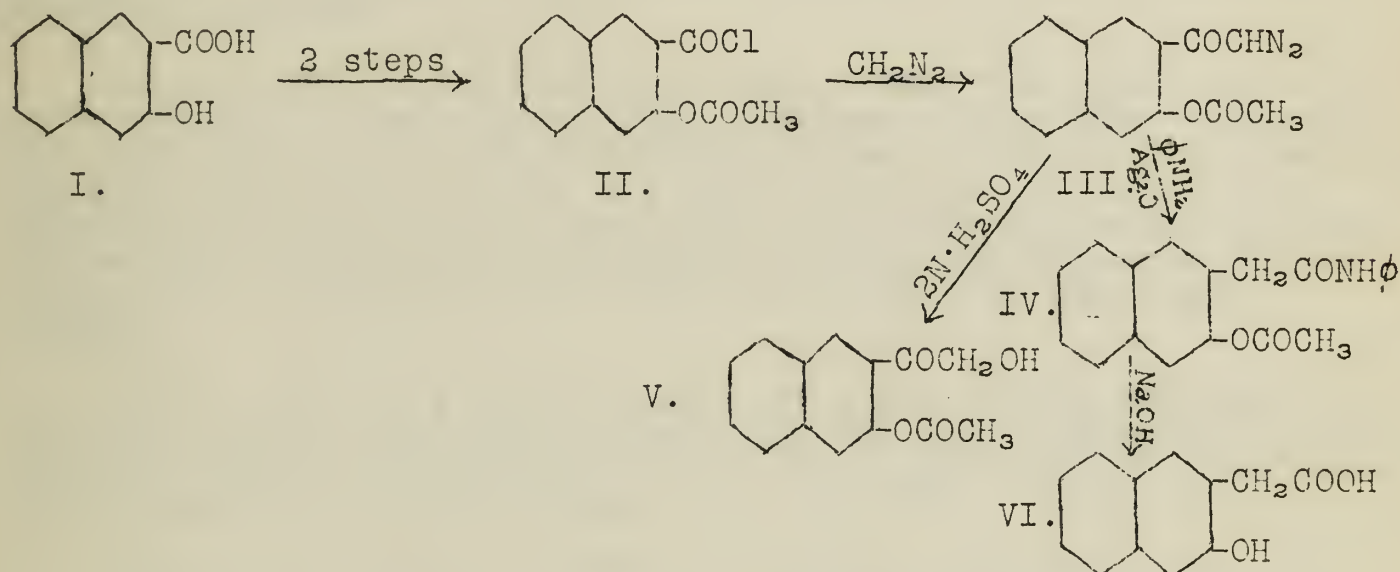
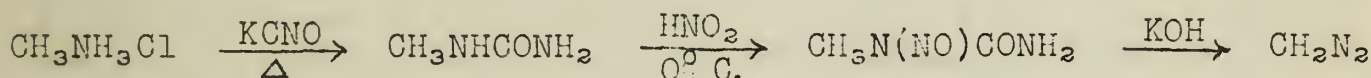
Arndt and co-workers developed an easy and inexpensive method of preparing diazomethane. Methyl urea, prepared by heating potassium cyanate with methylamine hydrochloride, gives, with nitrous acid, nitrosomethyl urea. Nitrosomethyl urea, in a suitable solvent with a 45 per cent potassium hydroxide solution, is converted into diazomethane.

Much earlier (1912) Wolff, in the preparation of diazoketones, oxidized phenyl glyoxal hydrazone with potassium permanganate, obtaining in good yield ω -diazoacetophenone. When he attempted to use ammoniacal silver nitrate as the oxidizing agent, he obtained, instead of the expected diazoketone, phenyl acetamide. Unable to explain this result, he subjected the diazoketone to the action of the ammoniacal silver nitrate, and found that phenyl acetamide was formed. This result led him to believe that the silver solution catalyzed a decomposition and subsequent rearrangement of the diazoketone. Wolff suggested the formation of a ketene as an intermediate in the reaction.

Arndt and Eistert, in 1935, correlated these various researches into a method for preparing the next higher homolog of an aromatic carboxylic acid. The acid chloride is prepared, and is added either directly or in solution to a cooled solution of diazomethane in a suitable solvent. The diazoketone is formed, and can be either isolated or used in the reaction mixture. A typical example is shown in the synthesis of 3-hydroxynaphthyl-2-acetic acid, as prepared by Eistert. 3-Hydroxy-3-naphthoic acid (I) is acetylated and then treated with thionyl chloride to give the acyl chloride (II). The diazoketone (III) is prepared by allowing the acyl chloride (II) (1 mol) in an ether solution to drop slowly into a cooled (10° C.) ether solution of diazomethane (2 1/2 mols). The anilide (IV) is prepared by treating the diazoketone (III) in alcoholic solution with aniline and freshly prepared silver oxide at $60-70^{\circ}$. The carbinol (V) is prepared by treating III in dioxan with 2 N sulfuric acid, and stirring for two hours. The free acid (VI) is prepared by saponifying IV with 2 N sodium hydroxide.

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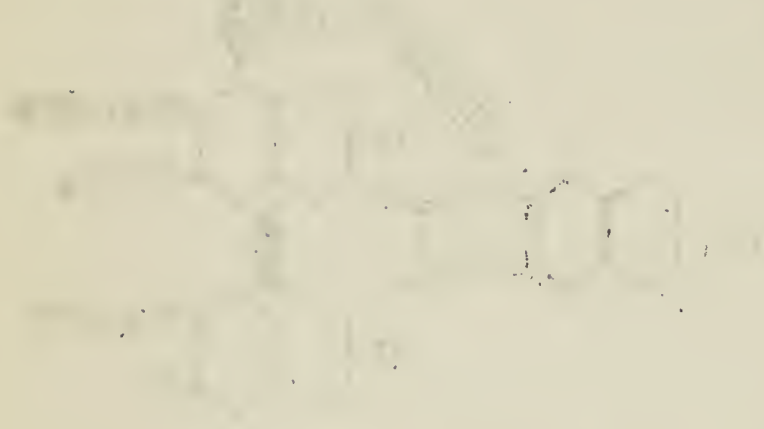
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AMMORESINOL

Kunz, Weidle and Fischer - Technical Institute
at Darmstadt.

Späth, Simon and Lintner - University of Vienna.

Raudnitz, Petru, Diamant, Neurad and Lanner -
University of Prague.

In 1924 Casparis isolated from gum ammoniacum a crystalline compound in the form of its diacetyl and dibenzoyl derivatives. The former on saponification gave a substance which was named ammoresinol, composed of colorless hexagonal crystals. The formula assigned to ammoresinol, $C_{18}H_{24}O_3$, was the same as that given by Luz in 1895. Ammoresinol has one phenolic group, as shown by a greenish brown color with ferric chloride which upon standing changes to reddish brown. It resinifies readily when exposed to light, air or a higher temperature, and on recrystallization except from benzene.

Kunz, Weidle and Fischer, in 1934, found that upon catalytic hydrogenation of ammoresinol they obtained a hexa hydro compound. Both the diacetyl and the dibenzoyl derivatives react with bromine. Six atoms are added and two are substituted. They report that oxidation of the diacetyl derivative with hydrogen peroxide yields γ -resorcylic acid while fusion with sodium and potassium hydroxides yields the β -resorcylic acid. They favored the formula $C_{24}H_{30}O_4$.

Späth, Simon and Lintner agree with the formula assigned by Kunz but because the methyl ether does not easily dissolve in cold aqueous alkali, believe that two of the oxygen atoms of ammoresinol are present in a lactone group.

They were, however, unable to isolate γ -resorcylic acid on degradation with hydrogen peroxide. Their analysis showed the product to be monoacetyl β -resorcylic acid, 2,4-HO(AcO) C_6H_3 COOH. By degradation of the diacetyl derivative they have obtained styphnic, 2,4,6-trinitro resorcinol, and β -resorcylic acid. Using potassium permanganate oxidation of the methyl ether they isolated 2,4-HO(MeO) C_6H_3 COOMe and 2,4-(MeO) $_2C_6H_3$ COOH.

By treating the hexa hydro compound with potassium permanganate in potassium hydroxide they obtained an oily acid which was obviously aliphatic in character and contained seventeen carbon atoms. Treating this hexahydro derivative with potassium permanganate in acetone gave: a ketone, 2,6-dimethyl undecanone; an acid lactone, 3,7,11-trimethyl-3-hydroxydodecane-1-carboxylic lactone; β -resorcylic acid and the monoacetyl β -resorcylic acid, 2-hydroxy-4-acetoxy benzoic acid.

Ozonization of the diacetyl derivative and treatment of the steam distillate of the ozonide decomposition products with semicarbazide gave the semicarbazone of 2-methyl-2-hepten-6-one. This suggested that the oily acid was made up of isoprene residues and, in fact, it was shown to be identical with 2,6,10-trimethyl-

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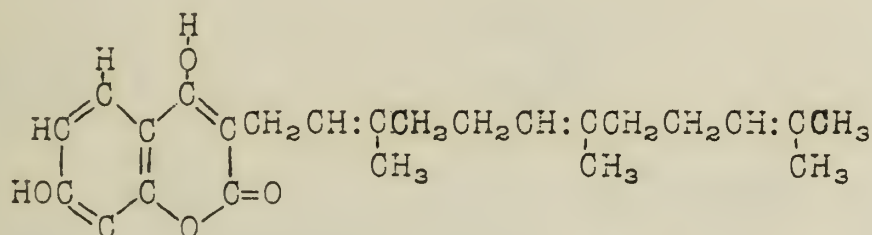
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tetradecan-14-oic acid, synthesized from 2,6,10-trimethyl pentadecan-14-one and which had been obtained from phytol by Willstätter, Schuppli and Mayer. The synthetic compound when mixed with the oxidation product gave no melting point depression.

Ammoresinol, on distillation under 0.3 mm., decomposed and yielded, resacetophenone and a compound $C_{10}H_8O_4$, found to be identical with synthetic 3-methyl-7-hydroxy benzotetronic acid. Therefore, ammoresinol is a 4-hydroxycoumarin. The double bond in this tautomerizable coumarin derivative is difficultly hydrogenated even after acetylation, as was shown by a control experiment on the acetylated 7-hydroxy benzotetronic acid; the saponified hydrogenation product split off water on distillation in a high vacuum and yielded umbelliferone. This explains why on normal catalytic hydrogenation only the three double bonds of the side chain are reduced. On the basis of the above results, ammoresinol is assigned the structure:



Raudnitz, et al., question Späth's results. They state that the oily acid was not pure and they could not cause the molecule to absorb more than three molecules of hydrogen. On oxidation with chromic anhydride they obtained two products, $C_{20}H_{20}O_8$ and $C_{22}H_{26}O_5$, these have not been more completely identified.

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Reported by J. H. Sample
 December 9, 1936.

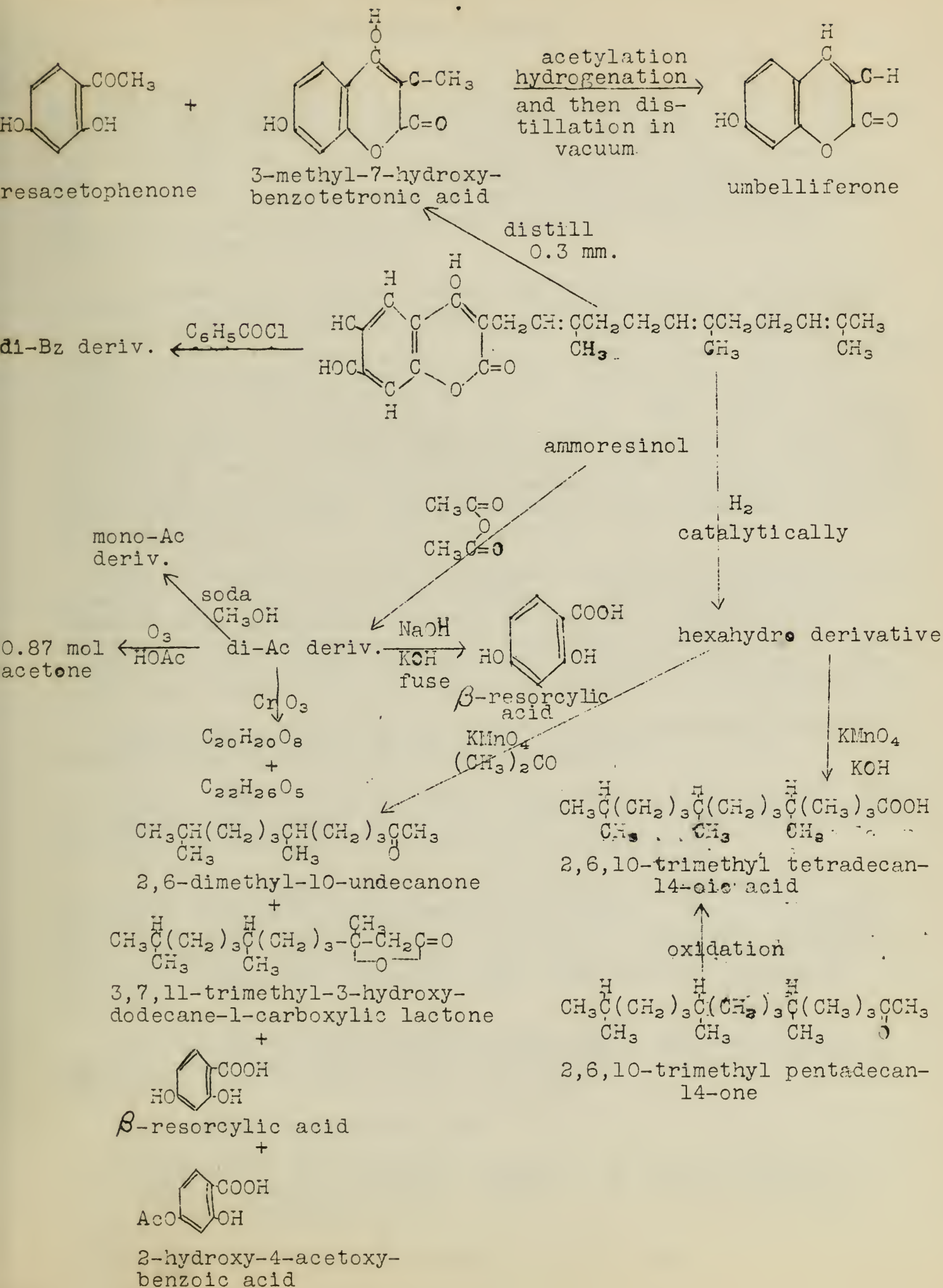




Diagram 1

Diagram 2

Diagram 3

Diagram 4

Diagram 5

Diagram 6

Diagram 7

Diagram 8

Diagram 9

Diagram 10

Diagram 11

Diagram 12

Diagram 13

Diagram 14

Diagram 15

Diagram 16

Diagram 17

Diagram 18

Diagram 19

Diagram 20

Diagram 21

Diagram 22

ADSORPTION ANALYSIS

The Russian botanist M. Tswett observed in 1906 that when a solution of a mixture of dyes is passed through a tube containing calcium carbonate the several components separate and appear as colored bands. He reported that several known plant pigments were composite in nature. Today the method is recognized as the best means of separating closely related or isomeric substances. The field of the polyene pigments was worked out accurately largely because of its use.

The technic is simple. Since the amounts which can be successfully separated rarely exceed a gram and usually vary from 1-10 mg. the tube may be from 10-60 mm. wide and 150-250 mm. in length. After fitting a porous plug in one end the tube is filled evenly with a prepared adsorbant. CaO , Ca(OH)_2 and CaCO_3 are ground to 300 mesh and dried at 150° . Al_2O_3 is prepared in several ways which yield different activities. The colored solution is drawn through by means of an aspirator and this is followed by more solvent which effects a better separation of the zones. The contents of the tube are then divided and the components extracted with a suitable solvent. Both the solvent and adsorbant must be selected empirically for each separation.

When the method is used to separate colorless substances the zones may be located by several means. Either the filtrate is tested as the zones move downward or they are marked off by observing their fluorescence in ultra-violet light. It is often possible to convert the substances to colored derivatives. The zones when once located are separated mechanically and extracted.

Successful separations of water soluble substances have been reported notably in the field of the flavines.

From a study of the reported separations it is observed that the greater the number of double bonds and the more oxygen in the molecule the stronger it is held by the adsorbant.

The method lends itself to determining rapidly whether a substance is pure or heterogeneous in nature. It is successful often when other methods fail, in particular chemical analysis. Some substances are altered by adsorption. Often this is due to traces of oxygen and peroxides which must be then carefully excluded.

The utility of the method has been amply demonstrated by results obtained by Kuhn, Karrer, Winterstein, Heilbrom and their workers.

Some notable separations are:

1. Separation of carotinoid pigments. γ -carotin separated from a mixture of 15% α -, 85% β -, and 0.1% γ -carotin. 1.7 mg. obtained.
2. Separation of α -, β -carotin. 10 mg. used.

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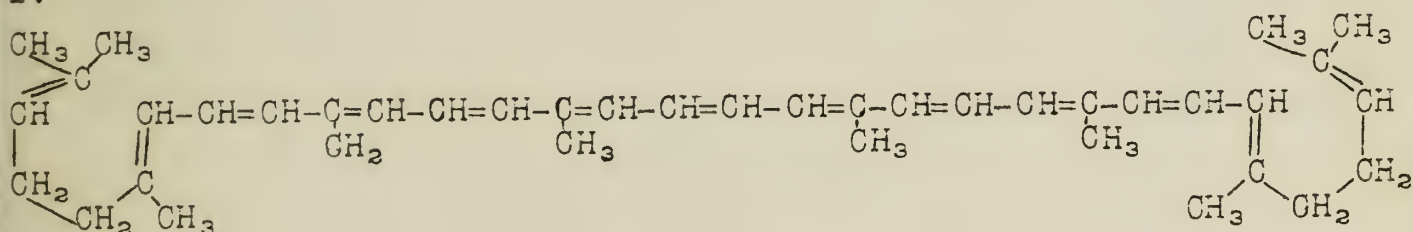
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3. Separation of chlorophyll (a) and (b) from leaf extracts. 3 g. of the mixture used. Yield 700 mg. pure chlorophyll (a), 1300 mg. chlorophyll (b) containing 10 per cent of (a).
4. Separation ergosterol from cholesterol. 5.6 mg. of the pro-vitamin in 20 g. of the cholesterol.
5. Purification of Vitamin A-extracts.
6. Ketones from hydrocarbons--an easy separation--Oleanol $C_{30}H_{47}OH$ and oleanylen $C_{30}H_{46}$, geraneol and limonene.
7. Tannins, anthocyanidins from plant extracts.
8. 1-Naphthol-4-sulphonic acid and 2-naphthol-4-sulphonic acid.
9. Uroflavine from urine.

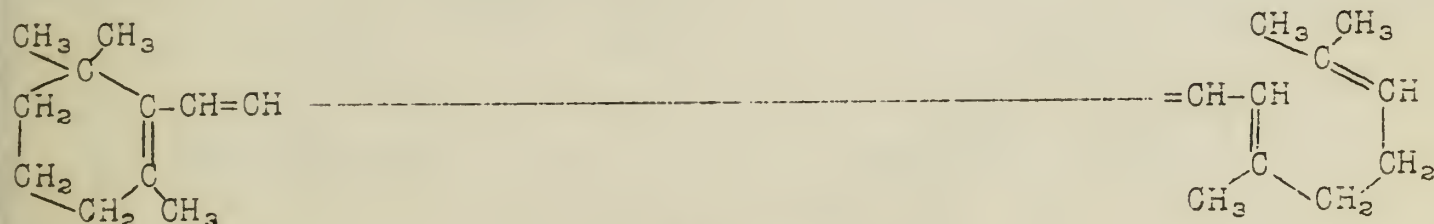
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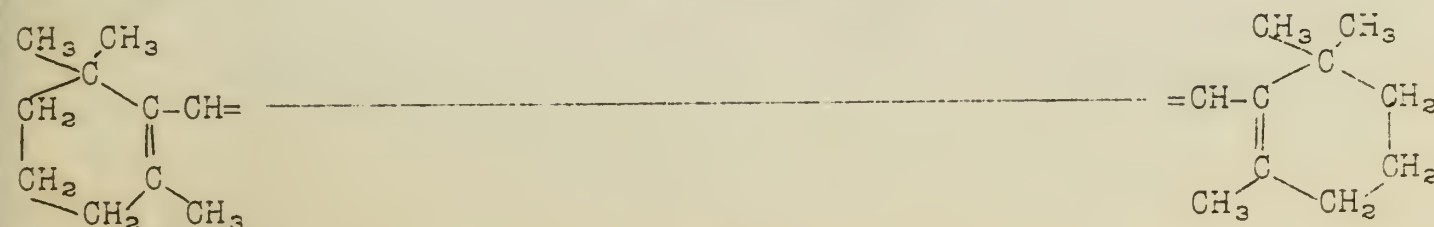
I.



I upper zone-lycopin



II. γ -carotin

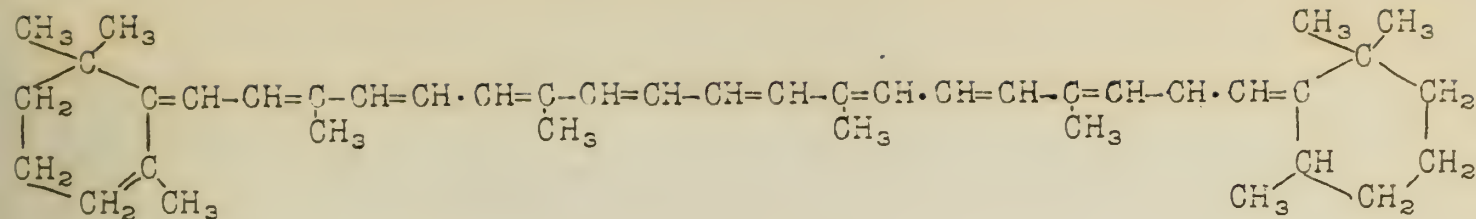


III. β -carotin

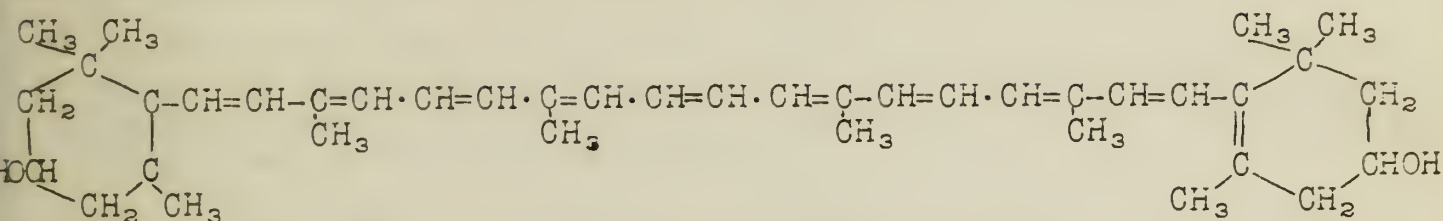
The first part of the paper is devoted to a general
 discussion of the problem. It is shown that the
 problem is equivalent to a problem in the theory of
 functions. The second part of the paper is devoted to
 a detailed study of the problem. It is shown that the
 problem is solvable in the case of a certain class of
 functions. The third part of the paper is devoted to
 a study of the properties of the solutions of the
 problem. It is shown that the solutions have certain
 properties. The fourth part of the paper is devoted to
 a study of the properties of the solutions of the
 problem. It is shown that the solutions have certain
 properties.

The fifth part of the paper is devoted to a study of
 the properties of the solutions of the problem. It is
 shown that the solutions have certain properties. The
 sixth part of the paper is devoted to a study of the
 properties of the solutions of the problem. It is shown
 that the solutions have certain properties. The seventh
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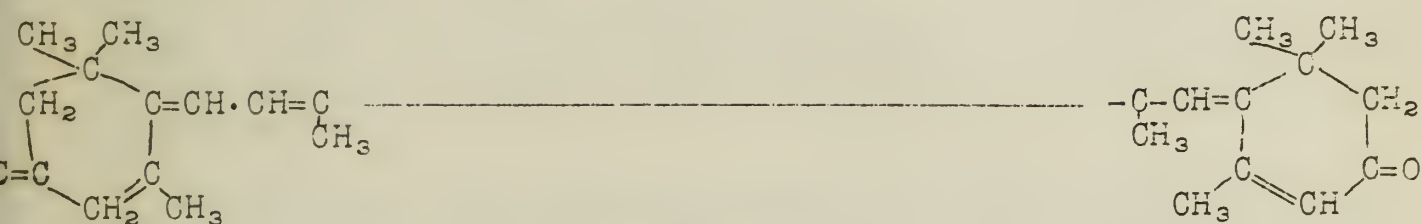
The ninth part of the paper is devoted to a study of
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IV. α -carotin

II.



Zeoxanthin 1st zone

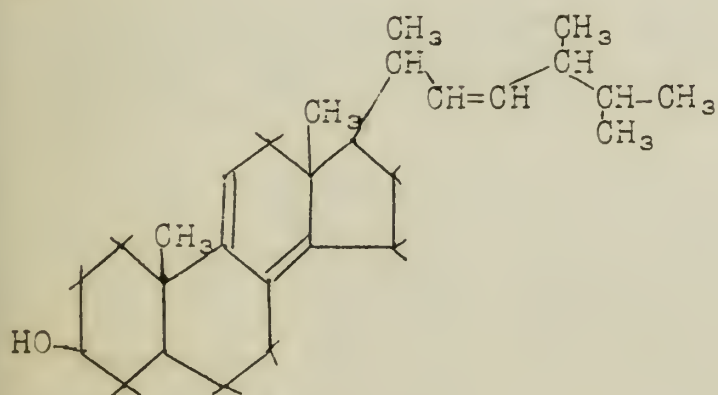


Rhodoxanthin

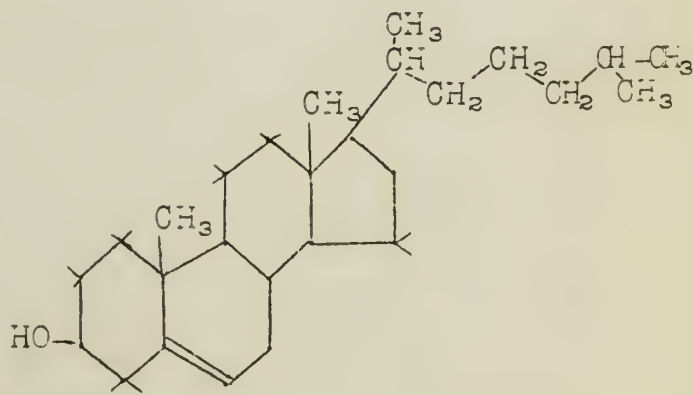


β -carotin

IV.



Ergosterol



Cholesterol

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117-119-11

117-119-11

117-119-11

117-119-11

117-119-11

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THE TRIPLE BOND IN
CARBOCYCLIC COMPOUNDS

Al. Favorsky, University of Leningrad
L. Ruzicka, Zürich

Rings containing a triple bond are not found in nature. Their interest derives from stereochemical considerations.

The first work of this particular nature was by Favorsky in 1912, in which 1,2-dibromo-1-chloro cyclohexane, upon treatment with alcoholic KOH and sodium in ether, gave only complex products with none of the desired acetylene.

Ruzicka points out that, according to the theory of strain, only rings of ten members or larger may contain a triple bond. He has synthesized cyclic acetylene of 15 and 17 members, but was unable to synthesize the 30 membered compound containing two triple bonds, since, he explains, the temperature required for cleavage of HBr was high enough to cause instantaneous rearrangement and condensation.

Comparison of the density of the acetylenes formed with the corresponding olefins and saturated hydrocarbons gives almost exactly the same variations observable in the aliphatic series.

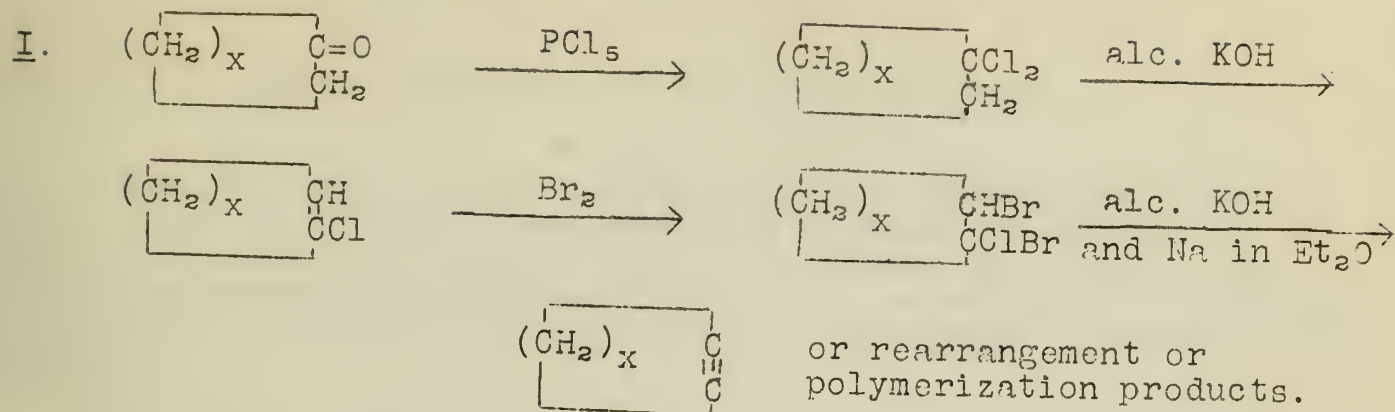
Favorsky carried out a series of experiments attempting to obtain the triple bond in rings of less than 10 members. The products resulting offer considerable interest.

In the five- and six-membered rings, polymerization products of the 1,3-dienes were obtained. Favorsky explains this by assuming that free radicals are first formed, that these then rearrange to allenes, and subsequently to 1,3-dienes.

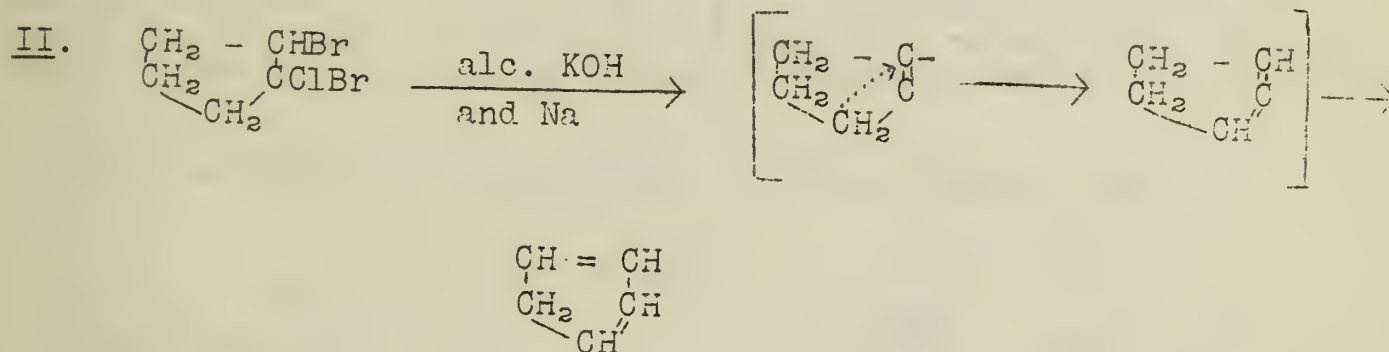
In the case of the seven-membered ring, this rearrangement stops at the allene stage. This ring appears to be large enough to take care of the strain of an allenic linkage. The structure was proved by ozonization, whereupon adipic acid was obtained.

The data variously recorded in the literature indicate that no acetylenic, allenic, or 1,3-dienic group is possible in the four-membered ring. The 5- and 6-membered rings may form the cyclopenta-1,3-diene and the cyclohexa-1,3-diene and the 1,4-diene, but the allene and the acetylene are impossible. In the 7-membered ring the acetylenic group is impossible, but the allene may be formed. In larger rings, Favorsky concludes that all forms of unsaturation are possible. He predicts that if cyclopropene were used and treated in the general way indicated above, diethynyl ethylene would be produced.

The general method of procedure was as follows:



Favorsky's suggestion concerning the mechanism of rearrangement is as follows:



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 Markownikoff, Ann., 327, 67 (1903)

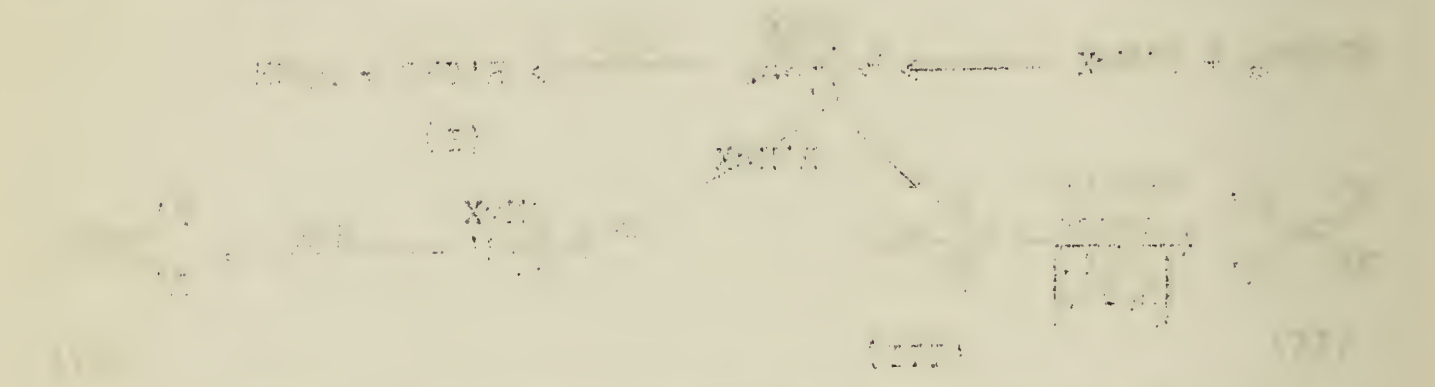
UNITED STATES DEPARTMENT OF AGRICULTURE

WATER RESOURCES DIVISION

REPORT OF THE COMMISSIONER OF THE GENERAL LAND OFFICE

The following is a list of the lands owned by the United States Government, and the amount of the same, as reported by the Commissioner of the General Land Office, for the year ending June 30, 1900.

The lands are classified as follows: (1) Lands owned by the United States Government, and (2) Lands owned by the States and Territories.

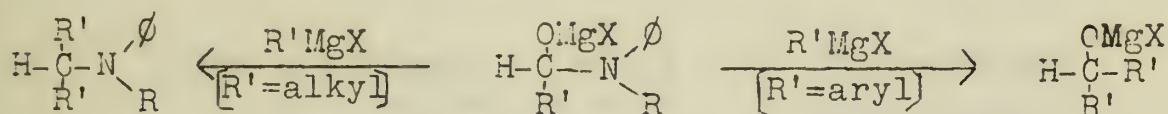


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When both positions R and R' are occupied by phenyl groups, the reaction leading to the tertiary amine (III) is blocked and the formation of the carbinol (IV) is favored. See example 7. The following choice of reaction is indicated:



Manner of hydrolysis: Ethylenic hydrocarbons were obtained only when the Grignard product was hydrolyzed in acid media. Cautious hydrolysis with ammonium chloride solution prevented any decomposition of the tertiary amine (III). Compare examples 4 and 5.

Previous work has shown that N-disubstituted amides other than formamides react with the Grignard reagent in a manner partially analogous to the reactions indicated above. Ketone formation is usually the predominant reaction, but tertiary amines and tertiary carbinols are sometimes obtained in good yields.

β -Substituted acids are obtained in good yields by 1,4-addition of the Grignard reagent to α,β -unsaturated N-disubstituted amides.

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7. Montagne and Isambert, Compt. rend., 203, 331 (1936)

EXAMPLES

Amide	Grignard Reagent	Products Isolated
(1) $\text{HCON}^{\text{Et}}_{\emptyset}$ (1 mol)	$\text{CH}_3\text{CHCH}_2\text{MgCl}$ (1 mol)	$\left\{ \begin{array}{l} \text{isovaleric aldehyde} - 36\% \\ \text{recovered amide} - 30\% \\ \text{tertiary amine} - 2\% \end{array} \right.$
(2) $\text{HCON}^{\text{Et}}_{\emptyset}$ (1 mol)	$\text{CH}_3\text{CHCH}_2\text{MgCl}$ (3 mols)	$\left\{ \begin{array}{l} \text{isovaleric aldehyde} - 24\% \\ \text{tertiary amine} - 50\% \end{array} \right.$
(3) $\text{HCON}^{\text{CH}_2\text{CH}_2\text{CH}_2}_{\text{CH}_2\text{CH}_2}$ (1 mol)	$\text{CH}_3\text{CHCH}_2\text{MgCl}$ (3 mols)	$\left\{ \begin{array}{l} \text{isovaleric aldehyde} - 6\% \\ \text{tertiary amine} - 75\% \end{array} \right.$

[illegible]

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<u>Amide</u>	<u>Grignard Reagent</u>	<u>Products Isolated</u>
(4) $\text{HCON} \begin{array}{l} \text{CH}_2\text{CH}_2 \\ \text{CH}_2\text{CH}_2 \end{array} \text{CH}_2$ (1 mol)	ϕMgBr (3 mols) (worked up with dil. H_2SO_4)	$\left\{ \begin{array}{ll} \text{benzaldehyde} & - \quad 11\% \\ \text{tetraphenyl-} & \\ \text{ethylene} & - \quad 76\% \end{array} \right.$
(5) $\text{HCON} \begin{array}{l} \text{CH}_2\text{CH}_2 \\ \text{CH}_2\text{CH}_2 \end{array} \text{CH}_2$ (1 mol)	ϕMgBr (3 mols) (worked up with NH_4Cl)	$\left\{ \begin{array}{ll} \text{benzaldehyde} & - \quad 11\% \\ \text{tertiary amine} & - \quad 63\% \end{array} \right.$
(6) $\text{HCON} \begin{array}{l} \phi \\ \text{CH}_3 \end{array}$ (1 mol)	ϕMgBr (3 mols)	$\left\{ \begin{array}{ll} \text{benzaldehyde} & - \quad 64\% \\ \text{benzhydrol} & - \quad 35\% \end{array} \right.$
(7) $\text{HCON} \begin{array}{l} \phi \\ \phi \end{array}$ (1 mol)	ϕMgBr (3 mols)	$\left\{ \begin{array}{ll} \text{benzaldehyde} & - \quad 9\% \\ \text{benzhydrol} & - \quad 88\% \end{array} \right.$
(8) $\text{HCON} \begin{array}{l} \text{Et} \\ \text{Et} \end{array}$	$\text{CH}_3\text{C}\equiv\text{C}-\text{MgBr}$	tertiary amine only $(\text{CH}_3\text{C}\equiv\text{C})_2\text{CHNEt}_2$
(9) $\text{C}_6\text{H}_4 \begin{array}{l} \text{CONEt}_2 \\ \text{OH} \end{array}$	$\text{C}_2\text{H}_5\text{MgBr}$	$\text{C}_6\text{H}_4 \begin{array}{l} \text{COCH}_2\text{CH}_3 \\ \text{OH} \end{array} \quad - \quad 82\%$
(10) $\phi\text{CH}=\text{CH}-\text{CON} \begin{array}{l} \text{CH}_3 \\ \phi \end{array}$	$\left\{ \begin{array}{l} \text{C}_2\text{H}_5\text{MgBr} \\ \phi\text{MgBr} \end{array} \right.$	$\phi\text{CH}-\underset{\text{R}}{\text{CH}_2}-\text{CON} \begin{array}{l} \text{CH}_3 \\ \phi \end{array}$ reported as "quali- tative yield"

Reported by Wayne Cole
December 16, 1936.

ORIENTATION IN THE NAPHTHALENE NUCLEUS

Ufimzew and coworkers (Dorogomilowsky Chemical Works,
Moscow)

Ber., 69, 2188 (1936)

J. prakt. Chem., (2) 140, 172 (1934)

(J. Allgem. Chem., 5, 653 (1935) Russ.

(Chem. Zentr., 1936, I, 768

Vesely and Jakes, Bull. Soc. chim., (4) 33, 954 (1923)

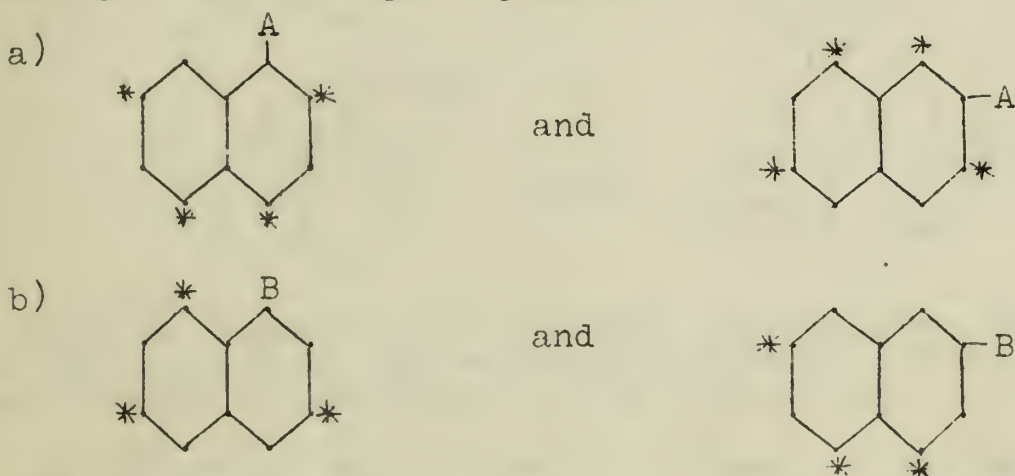
Armstrong and Wynne, J. Chem. Soc., 57, 130 (1890)

The question of orientation in the naphthalene series is complicated necessarily by the great number of substitution compounds, the still unresolved question of the mutual influence of the two rings and the dependence of the orientation on temperature (particularly in sulfonation).

As early as 1890, Armstrong and Wynne discovered the empirical rule that in sulfonation the entering group never occupied the ortho, para, or peri positions with respect to a group already present.

In 1923, Vesely and Jakes proposed the general rule that substituents could be divided into two classes: a) Those which direct ortho and para in the benzene nucleus and which orient in the naphthalene nucleus in such a way that they give disubstituted compounds in which the groups are in positions analogous to those of the oxygen atoms in the structurally possible naphthoquinones.

b) Those which direct meta in the benzene nucleus and which orient in the naphthalene nucleus to give disubstituted compounds not analogous to the naphthoquinones.



The conclusions of Vesely and Jakes agree with the electropolar theory.

Recent work has shown many exceptions to the above rules. Better orientation rules are obtained if naphthalene is considered to consist of an equilibrium mixture of the three forms--

STUDY OF THE ...

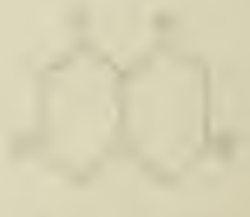
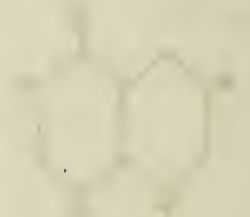
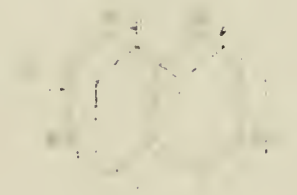
The first part of the study is devoted to a general description of the ...

The second part of the study is devoted to a detailed description of the ...

The third part of the study is devoted to a detailed description of the ...

The fourth part of the study is devoted to a detailed description of the ...

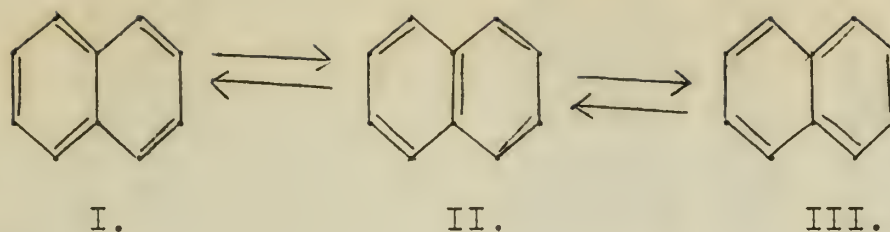
The fifth part of the study is devoted to a detailed description of the ...



The last part of the study is devoted to a detailed description of the ...

It is concluded that the study has shown that the ...

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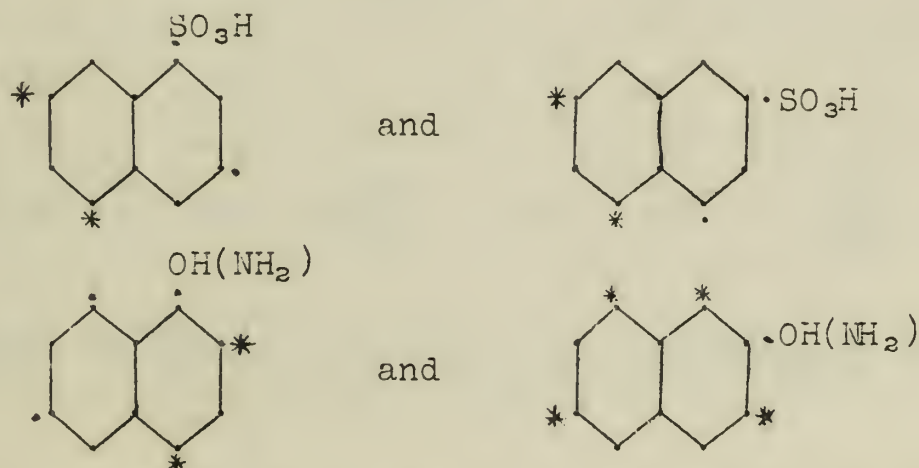


in which the equilibrium positions of the double bonds are displaced toward I and III by substitution. According to Ufimzew this conception of the naphthalene nucleus does not conflict in any way with any of its characteristic properties. Fieser has proved that such a condition does not exist in 2,7-dihydroxy-naphthalene.

With such a structure for naphthalene the group entering a monosubstituted naphthalene can enter in two ways: 1) It can enter the same ring as the first substituent subject to the ordinary rules for orientation in benzene nucleus.

2) It can enter the unsubstituted ring subject to the rules for orientation of the benzene ring with a substituted unsaturated closed side chain.

The predicted entering positions of the second group will then be as follows:



The asterisks represent the entering positions for the main products and the periods the entering positions for the products formed through orientation into the other ring.

The following table contains a summary of reliable data concerning the orientation of monosubstituted naphthalenes. The few exceptions to the above predictions are analogous to the few anomalous cases of orientation in the benzene nucleus. The under-scored positions designate main products.



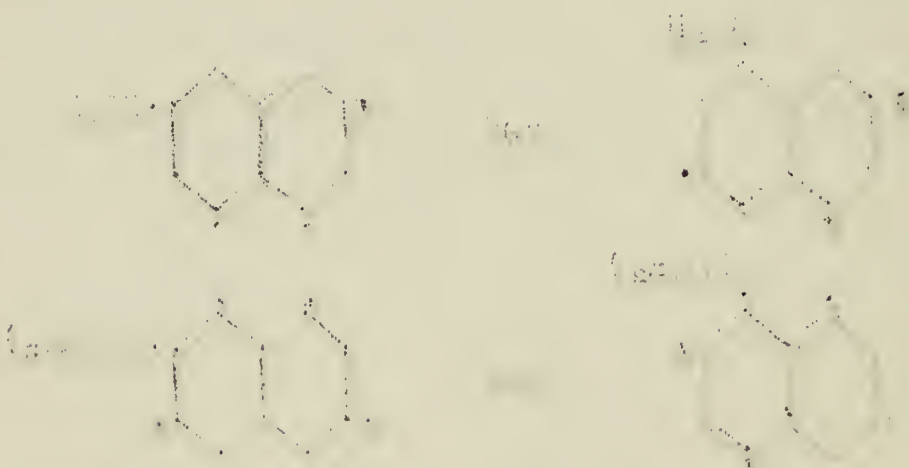
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The first isomer is a naphthalene-like molecule with a double bond in the bridgehead position. The second isomer is a similar molecule with the double bond in a different bridgehead position. The third isomer is a similar molecule with the double bond in a third bridgehead position. They are connected by equilibrium arrows.

The first isomer is a naphthalene-like molecule with a double bond in the bridgehead position. The second isomer is a similar molecule with the double bond in a different bridgehead position. The third isomer is a similar molecule with the double bond in a third bridgehead position. They are connected by equilibrium arrows.

The first isomer is a naphthalene-like molecule with a double bond in the bridgehead position. The second isomer is a similar molecule with the double bond in a different bridgehead position. The third isomer is a similar molecule with the double bond in a third bridgehead position. They are connected by equilibrium arrows.

The first isomer is a naphthalene-like molecule with a double bond in the bridgehead position. The second isomer is a similar molecule with the double bond in a different bridgehead position. The third isomer is a similar molecule with the double bond in a third bridgehead position. They are connected by equilibrium arrows.



The first isomer is a naphthalene-like molecule with a double bond in the bridgehead position. The second isomer is a similar molecule with the double bond in a different bridgehead position. The third isomer is a similar molecule with the double bond in a third bridgehead position. The fourth isomer is a similar molecule with the double bond in a fourth bridgehead position. They are connected by equilibrium arrows.

The first isomer is a naphthalene-like molecule with a double bond in the bridgehead position. The second isomer is a similar molecule with the double bond in a different bridgehead position. The third isomer is a similar molecule with the double bond in a third bridgehead position. The fourth isomer is a similar molecule with the double bond in a fourth bridgehead position. They are connected by equilibrium arrows.

First Substituent and its Position		Second Substituent and its Entering Position						Remarks	
		SO ₃ H		NO ₂		Cl			Br
		Main Pro-ducts	By-Pro-ducts	Main Pro-ducts	By-Pro-ducts	Main Pro-ducts	By-Pro-ducts		
Substituents which would orient <u>meta</u> in the benzene ring.	SO ₃ H	5	6	8	5, 4	5	5	Sulfonation at low temp. Sulfonation at high temp.	
	CO ₂ H	5, 7	6	5	8	5	5		
	CN	5?		5	5, 3	5	5		
	NO ₂	5	3	3		3	5, 8		
	SO ₃ H	7	6	5	3	5	5		
	CO ₂ H	5	8	5	8				
	NO ₂								
Substituents which would orient <u>ortho</u> and <u>para</u> in the benzene ring.	CH ₃	4	5	4	5, 3			Sulfonation and nitration without excess H ₂ SO ₄ Sulfonation and nitration with excess H ₂ SO ₄ Nitration in large excess H ₂ SO ₄ Sulfonation at low temp. Sulfonation at high temp. Low temp. High temp.	
	Cl	4		4		2, 4	4		
	Br	4		4		2, 4	4		
	OH	2, 4	5, 6	2, 4	8				
	OC ₂ H ₅	4	4, 6	5					
	O·CO·CH ₃	5		3, 4		2, 4			
	NH ₂	5		2, 4					
	NH·CO·CH ₃	4	5	3, 4					
	N(CH ₃) ₂	5		1		1	1		
	CH ₃	6, 8		1, 6, 8					
	Cl	1		5					
	OH	8, 9		5					
	OH	1		6, 8					
	OCH ₃	8, 6	5	1, 6, 8					
	NH ₂	9	7	5					
	NH·CO·CH ₃	6		1					
	NH·CO·CH ₃	6		1					

1. The first part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

2. The second part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

3. The third part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

4. The fourth part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

5. The fifth part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

6. The sixth part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

7. The seventh part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

8. The eighth part of the document is a list of names and their corresponding addresses. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into two columns, with names on the left and addresses on the right.

CONSTITUTION AND SYNTHESIS OF LAPACHOL:

HOOKER'S OXIDATION

Hooker, J. Am. Chem. Soc., 58, 1163 (1936)
 " , Am. Chem. J., 11, 267 (1889)
 " , " " " , 11, 393 (1889)
 " , J. Chem. Soc., 61, 611 (1892)
 " , " " " , 63, 424 (1893)
 and various other articles by Hooker.
 Fieser, J. Am. Chem. Soc., 49, 857 (1927)
 " , " " " " , 58, 1223 (1936)

Other work: Structure of Retene

Hooker obtained his Ph. D. from Munich in 1885, and shortly afterwards was employed by the Franklin Sugar Refining Company in the United States. For several years (1889-1896), he spent his leisure time working on the structure of lapachol; but in 1896, because increasing duties in the industrial field required too much of his time, he was forced to abandon his research on lapachol until 1915. At that time, he retired from business and turned again to his study of lapachol. The results of twenty years of research (1915-1935) were disclosed last July, when in one issue of the Journal Dr. Hooker contributed eleven papers.

As early as 1857, Arnoudon reported under the name of taiguc acid a yellow coloring matter existing in the Taigu wood of Paraguay. In 1863, Stein described greenbartin, a yellow coloring matter existing in Surinam greenbart. Paternø (1879) proved that lapachoic acid (lapachol) isolated by Siervert from the Lapacho tree of South America was identical with the above coloring matters. Still later, Hooker (1889) reported the isolation of lapachol from Bethabarra wood of South Africa.

Early investigations by Paternø and Hooker showed that lapachol (I) was an amylenehydroxynaphthaquinone. The structure was based on the following experimental data:

- 1) Lapachol on distillation with Zn dust yields naphthalene and isobutylene.
- 2) Oxidation with nitric acid yields phthalic acid in amounts sufficient to show that all side groups are situated in the same benzene ring.
- 3) Reduction with HI was thought to give amyl naphthalene.
- 4) It formed a monoacetyl derivative.
- 5) Formation of metallic salts.

UNITED STATES DEPARTMENT OF AGRICULTURE
BUREAU OF PLANT INDUSTRY

REPORT OF THE
COMMISSIONER OF PLANT INDUSTRY
FOR THE YEAR 1907

WASHINGTON, D. C., 1908

THE COMMISSIONER OF PLANT INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE, has the honor to acknowledge the receipt of the report of the COMMISSIONER OF PLANT INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE, for the year 1907. The report is a valuable contribution to the knowledge of the plant industry of the United States, and is a most interesting and instructive work. It contains a detailed account of the progress of the plant industry during the year, and a summary of the work of the Bureau of Plant Industry. The report is divided into two parts, the first of which contains a general account of the plant industry, and the second of which contains a detailed account of the work of the Bureau of Plant Industry. The report is a most valuable contribution to the knowledge of the plant industry of the United States, and is a most interesting and instructive work. It contains a detailed account of the progress of the plant industry during the year, and a summary of the work of the Bureau of Plant Industry. The report is divided into two parts, the first of which contains a general account of the plant industry, and the second of which contains a detailed account of the work of the Bureau of Plant Industry.

-2-

- 6) Similarity of lapachol to hydroxy- α -naphthaquinones with respect to color and volatility, and the similarity of β -lapachone III to α -naphthaquinones, also led Hooker to assign an α -quinone group to lapachol. This assignment, naturally, places the hydroxy group and the amylene group in the β positions.

Only the structure of the amylene side-chain remained to be determined. Hooker tentatively proved this side-chain to be

$-\text{CH}_2 \cdot \text{CH}=\text{C} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix}$ by preparation of isolapachol (XIII) and the conversion of it and lapachol into the same compounds. Later (1936) Hooker was able definitely to show that lapachol contained the side-chain indicated by the preparation of dihydrolapachol (II) from both isolapachol (XIII) and lapachol. Also by a method of degradation, Hooker converted lapachol into its next lower homolog, and demonstrated that the side-chain skeleton was that of formula (a).

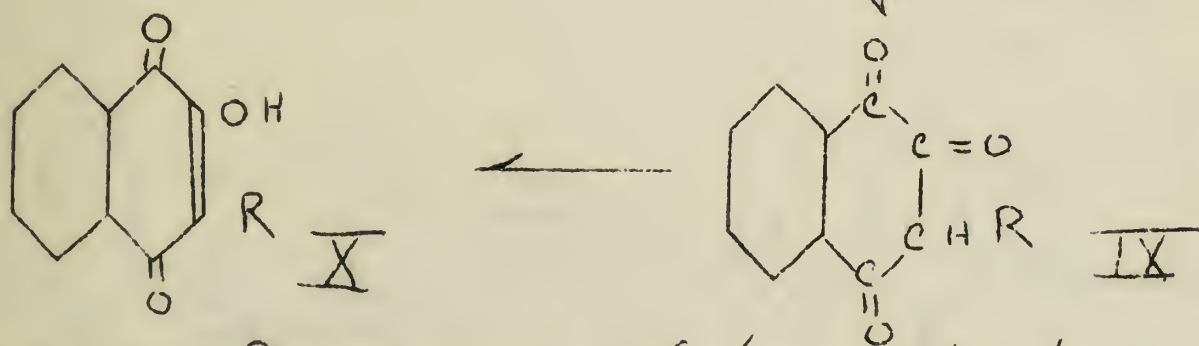
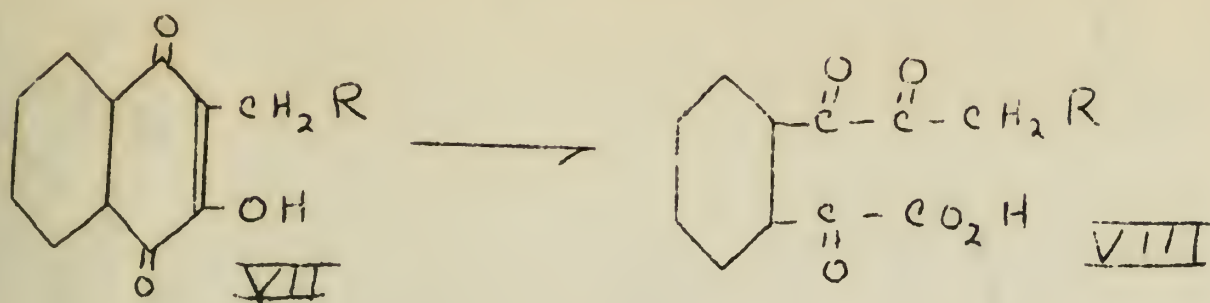
In the course of Hooker's work on lapachol, he studied its oxidation with alkaline permanganate solution; the results were entirely unexpected, indeed, surprising.

Lapachol when oxidized with alkaline permanganate yields a new compound which has lost a (CH_2) group from the side-chain leaving the remainder of the side-chain $\left(\text{CH}=\text{C} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} \right)$ attached to the quinone ring. This reaction proved to be not only an excellent method of degrading lapachol, but to be general when other derivatives of 2-hydroxy-1,4-naphthaquinone were used. The reaction has been designated as the Hooker oxidation (see V and VI). The mechanism for this oxidation is outlined on the abstract sheets (see VII-X), and it has been confirmed by Fieser.

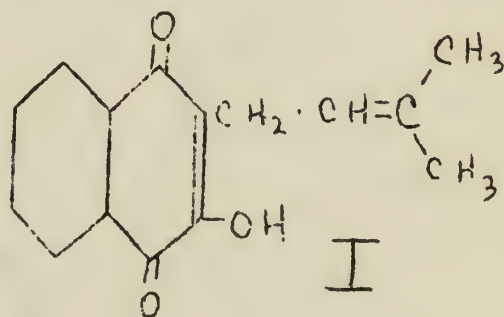
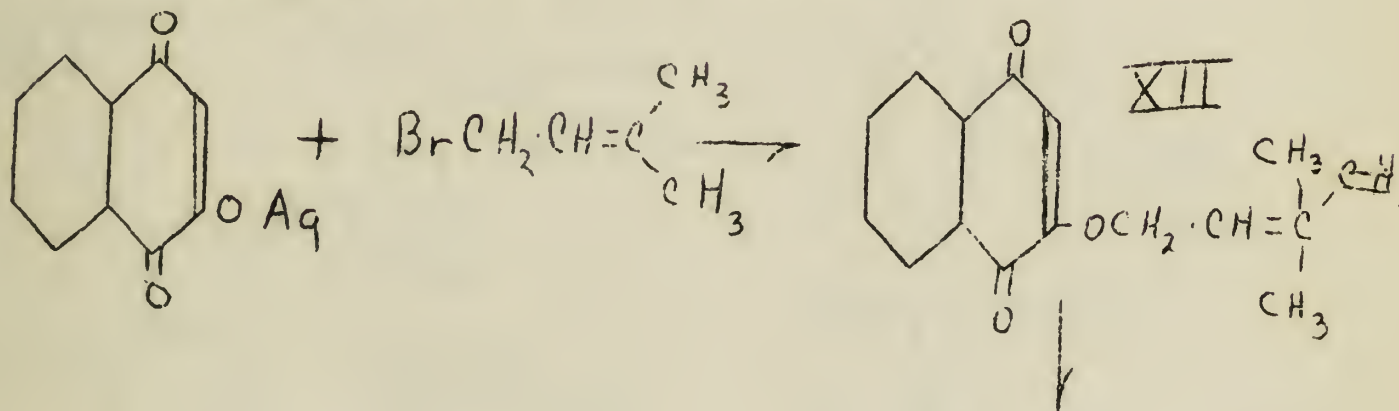
Finally, Fieser and Hooker have both synthesized lapachol, thereby proving its structure as predicted by Hooker.

Mechanism of Oxidation

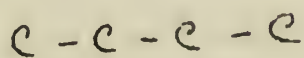
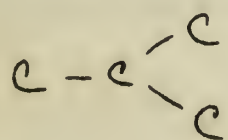
63



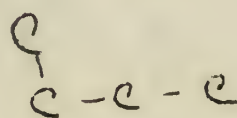
Feiser's Synthesis of Lapachol



Skeleton Structures



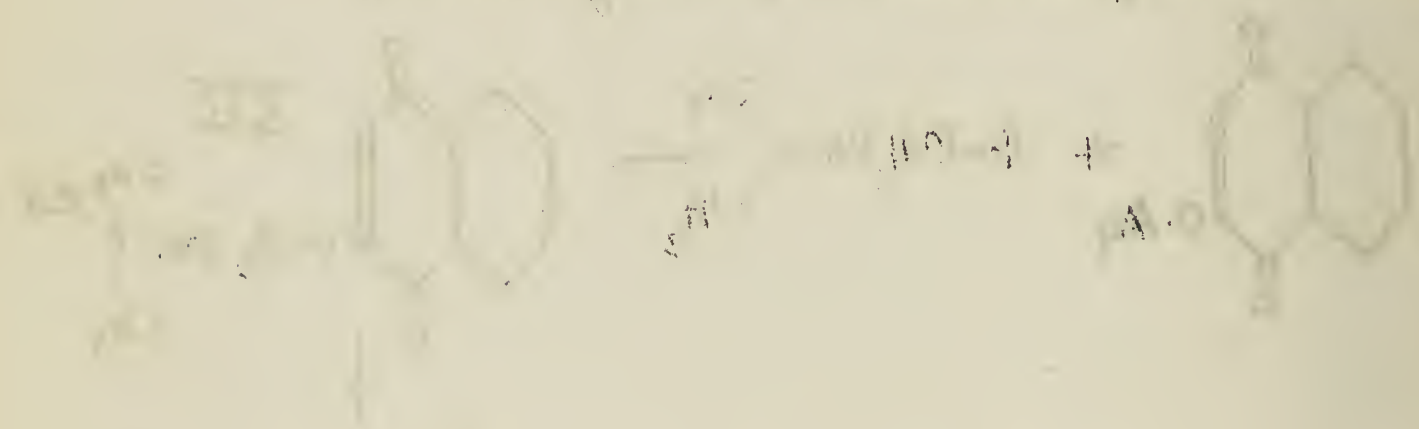
(b)



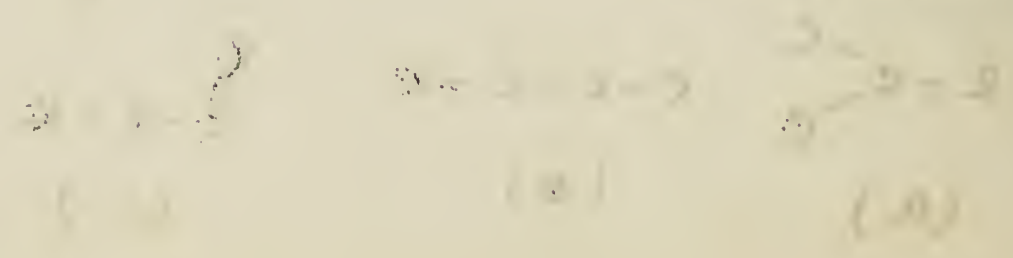
(c)



Reaction of monomers of cellulose

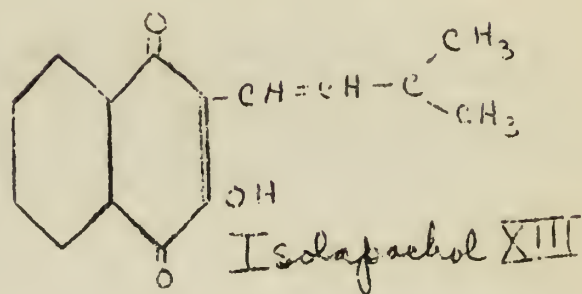
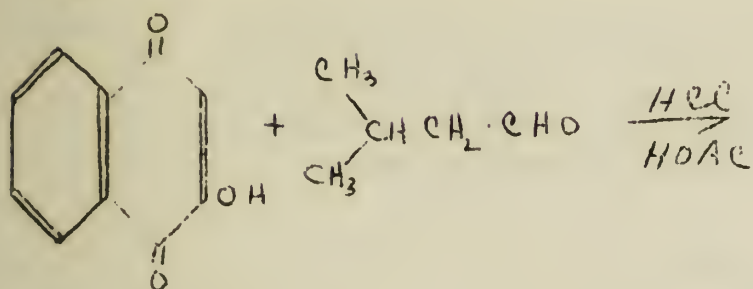
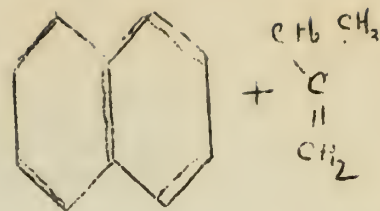
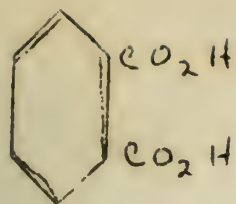


Reaction of monomers of cellulose

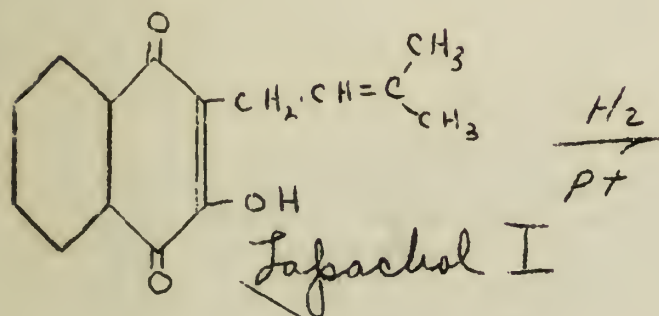
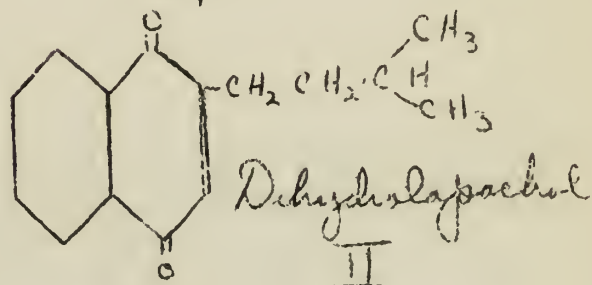


$\xrightarrow{HNO_3}$ Lapachol

$\xrightarrow[\Delta]{Zn}$



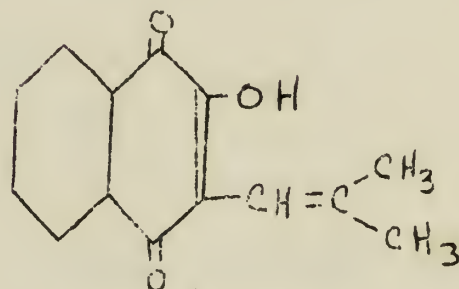
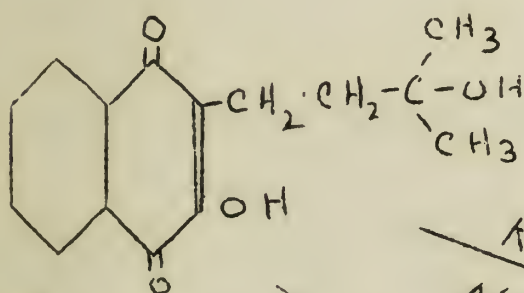
$\xrightarrow[\text{Pt}]{\text{H}_2}$



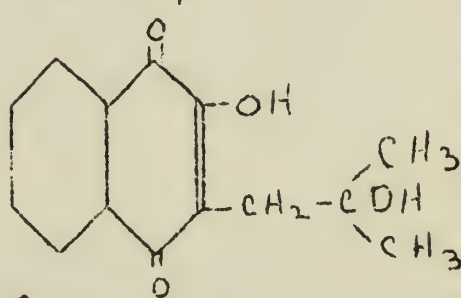
$\xrightarrow[\text{NaOH}]{\text{H}_2\text{SO}_4}$

$\xrightarrow{\text{KMnO}_4}$

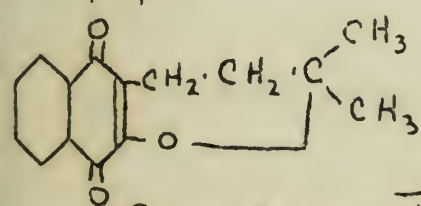
$\xrightarrow{\text{NaOH}}$



$\xrightarrow[\text{NaOH}]{\text{H}_2\text{SO}_4}$

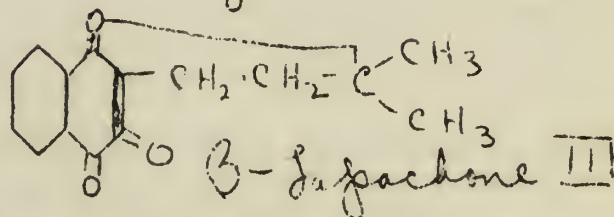


$\xrightarrow[\text{HCl}]{\text{NaOH}}$

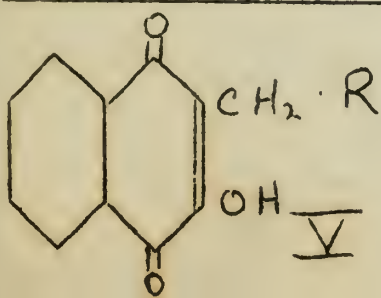


$\xrightarrow[\text{NaOH}]{\text{KMnO}_4}$

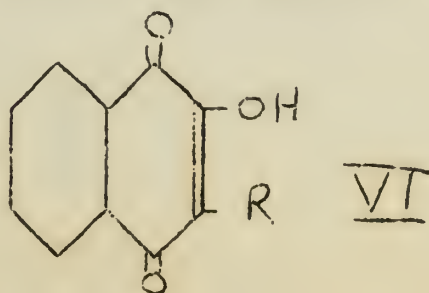
$\xrightarrow[\text{NaOH}]{\text{H}_2\text{SO}_4}$

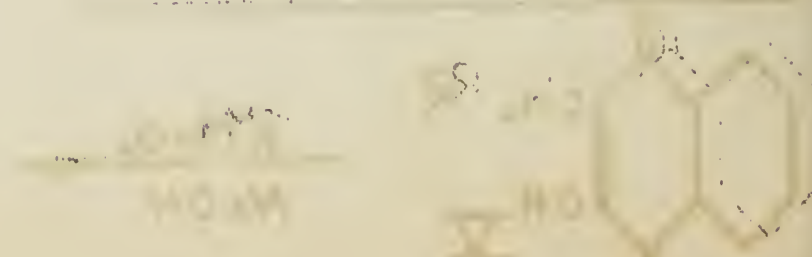
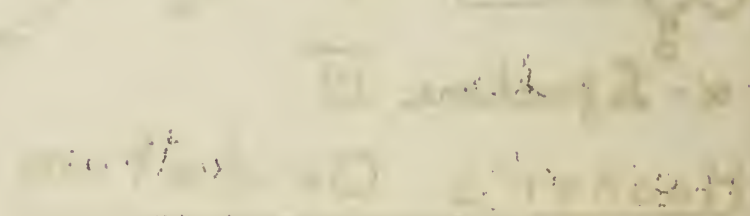
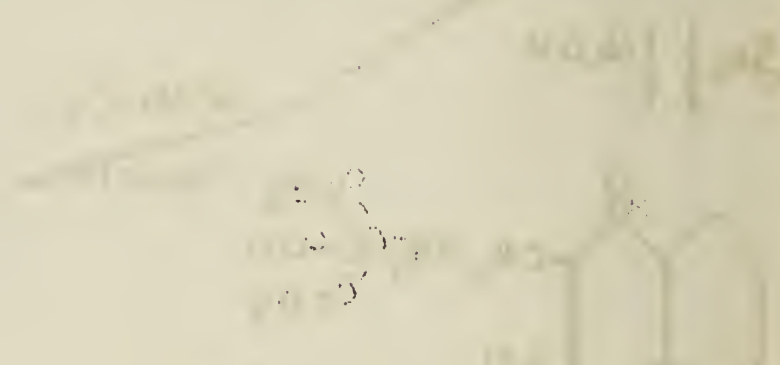
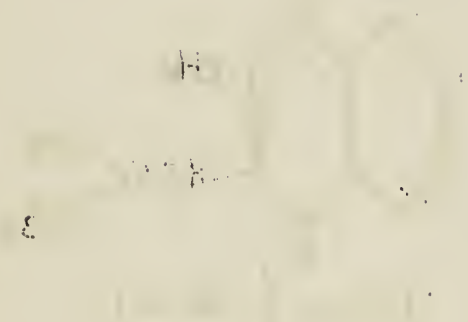
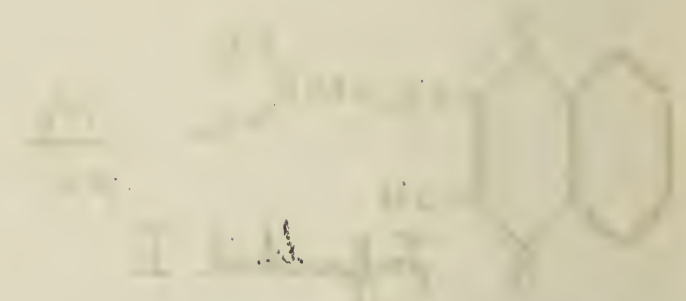
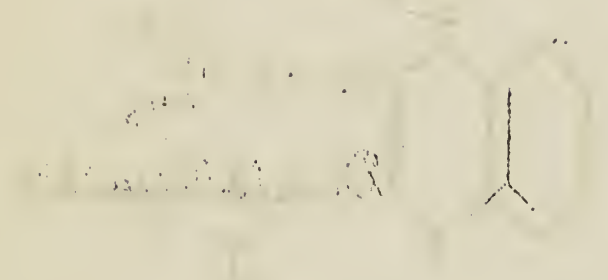
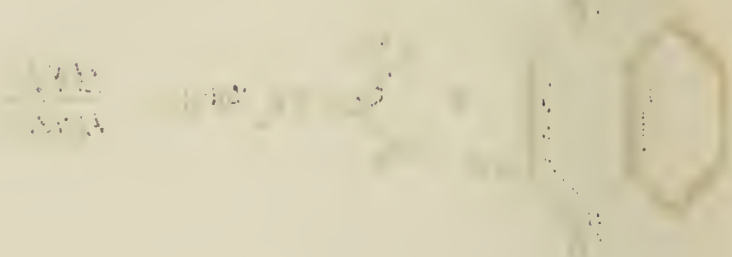
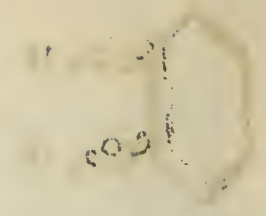


Hooker's Oxidation



$\xrightarrow[\text{NaOH}]{\text{KMnO}_4}$

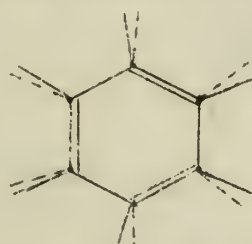




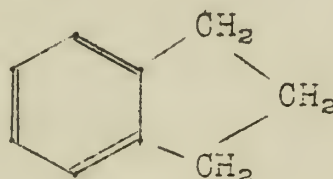
MILLS-NIXON EFFECT

Mills and Nixon -- Cambridge University
 Sidgwick and Springall -- Oxford University
 Fieser et al -- Harvard University

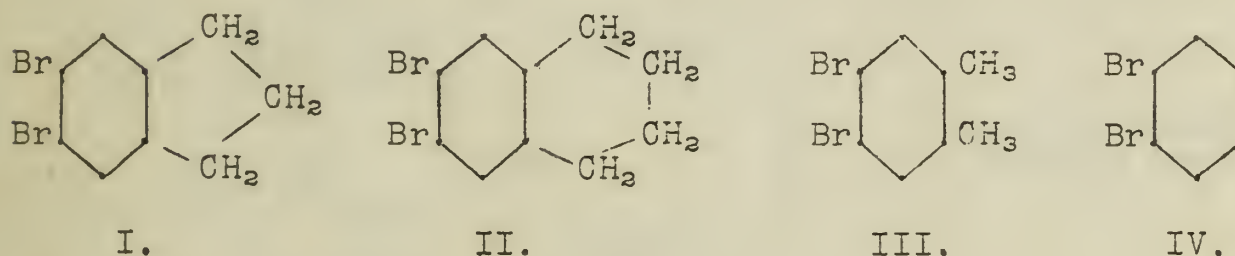
Theory: Assuming the tetrahedral character of the carbon atom and the Kekulé structure for benzene it appears that the external valencies of the carbon atoms in the benzene nucleus would not be directed as if from the center of a hexagon but would be bent slightly to the side away from the double bond.



A force which would tend to push apart or bring closer together any adjacent pair of the external valence radii should also tend to make the nuclear double bonds immobile, thus fixing the structure of the benzene ring. Such a restricting force is the five-membered alicyclic ring in hydrindene, the structure of which must be:

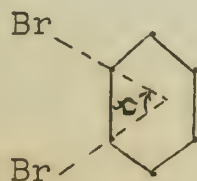


Proof: Dipole moment determinations of Sidgwick and Springall:

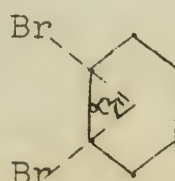


μ	for Br-C-C-Br fragment in 5,6-dibromohydrindene (I)	1.78 D
μ	" " " " 6,7-dibromotetralin (II)	2.11
μ	" " " " 4,5-dibromo-o-xylene (III)	2.13
μ	" " " " 1,2-dibromobenzene (IV)	2.12

The values show that in 5,6-dibromohydrindene the central angle, $\angle C$, is ~~less~~ ^{more} than 60° ; but equal to 60° , at least as an average value, in the halogenated tetralin, xylene and benzene.



I.



II, III, and IV.

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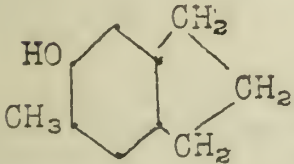
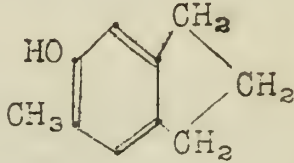
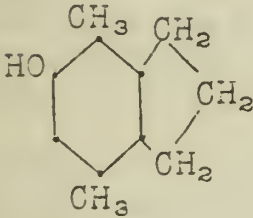
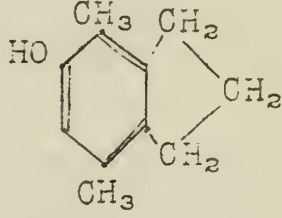
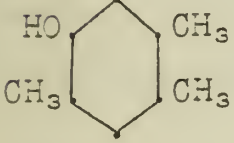
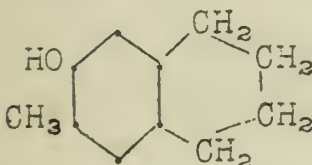
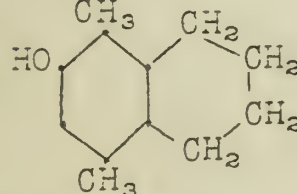
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Chemical evidence of Fieser and Lothrop:

Fieser has employed the coupling reaction of phenols with diazonium compounds to determine the position of the double bonds in phenanthrene, anthracene and naphthalene. If the para position in the phenol is blocked, coupling occurs in the ortho position involved in the enolic system.

The reaction was applied to the hydrindene problem with the following results:

Compound	Reaction with 	Structure
	None	
	Coupling	
	Coupling	Mobile system of conjugated double bonds
	Coupling	Mobile system of conjugated double bonds
	Coupling	

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Proof of theory by dipole moments:

Sidgwick and Springall, J. Chem. Soc., 1532 (1936)

Proof of theory by coupling reactions:

Fieser and Lothrop, J. Am. Chem. Soc., 58, 2050 (1936)

The chemical structure of ... is shown in the figure. It is a ... of ... and ... The ... of ... is ... The ... of ... is ...

The chemical structure of ... is shown in the figure. It is a ... of ... and ... The ... of ... is ... The ... of ... is ...

The chemical structure of ... is shown in the figure. It is a ... of ... and ... The ... of ... is ... The ... of ... is ...



The chemical structure of ... is shown in the figure. It is a ... of ... and ... The ... of ... is ... The ... of ... is ...

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 " " " " , 58, 543 (1936)
 " " " " , 58, 1991 (1936)
4. Pfeiffer, J. Prakt. Chem., 126, 97 (1930)
5. Errea and Mollet, Compt. rend., 200, 814 (1935)

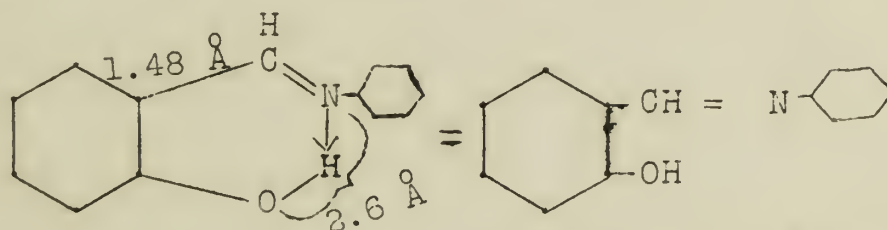
Although the hydrogen bond was postulated by Latimer and Rodebush in 1920 to explain the high dielectric for hydrogen fluoride, its greatest application by far has been with organic molecules.

Sidgwick rightly assumed that in many cases anomalous molecular weights were due primarily to the formation of hydrogen bonds through a semi-polar (or coordinate covalent) link. Such a ring, i. e., one containing a semi-polar bond, is often designated in a chelate ring. The work of Kumler (California) has showed without doubt that hydrogen bonds exist and proved their effect on the dielectric constant, boiling point, etc.

The most recent and obviously the most exact measurement in the determination not only of the presence but also the concentration of hydrogen bonds has been infra-red absorption spectra. The absence of "OH" or ">NH" absorption bands in molecules where these are known to exist (by chemical reactions) is taken as a criterion for hydrogen bond formation.

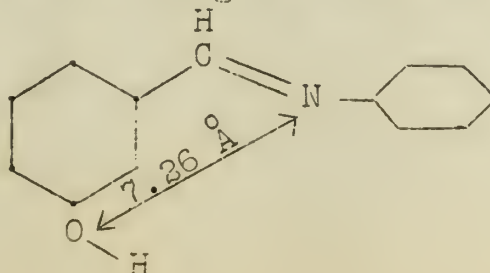
The rules for hydrogen bond formation can be stated as follows:

- I. The distance between an "O" atom in a hydroxyl group and an "N" atom with which the hydrogen is coordinated must be about 2.6 Å. Thus,



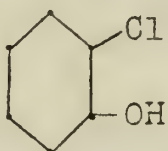
A chelate ring here is favored

However, the distance between the oxygen and nitrogen atoms in the following example is too large to allow chelation.

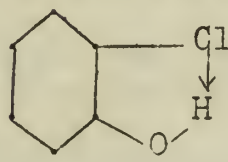


-2-

- II. The ring should have minimum number of >C-C< about which free rotation is possible.
- III. The entire system must be strain free. This involves in oxygen compounds in most cases a six-membered ring.

For example in  the strain caused

by the formation of a chelate ring to give

 prevents this form from being a stable configuration.

Reported by R. T. Arnold
January 6, 1936.

THE UNIVERSITY OF CHICAGO

DEPARTMENT OF CHEMISTRY

THEORY



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RELATIVE REACTIVITIES OF
ORGANO METALLIC COMPOUNDS

69

Gilman and coworkers, Iowa State College

J. Am. Chem. Soc.,	47,	2002	(1925)
" " " "	, 55,	1265	(1933)
" " " "	, 56,	1415	(1934)
Rec. trav. chim.,	49,	212	(1930)
" " " "	, 54,	584	(1935)
" " " "	, 55,	76, 133, 518, 561, 577,	
		585	(1936)
Jour. Org. Chem.,	1,	315	(1936)

The reactivities of the organo compounds of the first three groups of the periodic table are of the following order:

$\text{Cs} > \text{Rb} > \text{K} > \text{Na} > \text{Li} > \text{Ca} > \text{Mg} > \text{Al} > \text{B} > \text{Zn} > \text{Cd} > \text{Cu} > \text{Ag} > \text{Hg} > \text{Au}.$

This is roughly the same order in which these metals occur in the E. M. F. series, exceptions being Li and Ca.

The term "reactivity" as used here refers to the ability of the organo-metallic compound to react with some such grouping as $-\text{C}=\text{O}$ or $-\text{C}\equiv\text{N}$, and not to the thermal instability or spontaneous inflammability of the compound.

In establishing this order of reactivities the following reactions were made use of:

1. Metalation by means of RM or RMX
2. Rate of reaction of RM or RMX with benzonitrile
3. Length of time taken for RM or RMX to produce a color with Michler's ketone
4. Rate of reaction of *n*-butyl chloride with ketyls
5. Addition or non-addition of RM or RMX to unsaturated compounds.

Organo derivatives of Cs, Rb, K, Na, Li and Ca will metalate dibenzofurane; RMgX and the remaining RM compounds of the metals listed in the table will not. Potassium ethyl and sodium ethyl yield dimetalated dibenzofurane. Potassium ethyl yields more dimetalated dibenzofurane than does sodium ethyl. Lithium ethyl yields only monometalated dibenzofurane. These facts coupled with the rates of reactions of the phenylacetylenyl derivatives of the alkali metals with benzonitrile, and with the rates of reactions of the benzophenone ketyls of the alkali metals with *n*-butyl chloride place the metals in the preceding order.

Organo derivatives of Cs, Rb, K, Na, Li, Ca, Mg, Al, B, Zn and Cd give color tests with Michler's ketone. The remaining RM compounds in the list do not. The time required for the production of color with the last five of this list are in the following order:

$\text{Mg} < \text{Al} < \text{B} < \text{Zn} < \text{Cd}.$

2. The second part of the paper discusses the role of the state in the development of the economy.

1. The first group of people who are interested in the study of the history of the world are the historians. They are the people who study the past and write about it. They are the people who tell us what happened in the past and why it happened. They are the people who help us to understand the world we live in today.

[illegible]

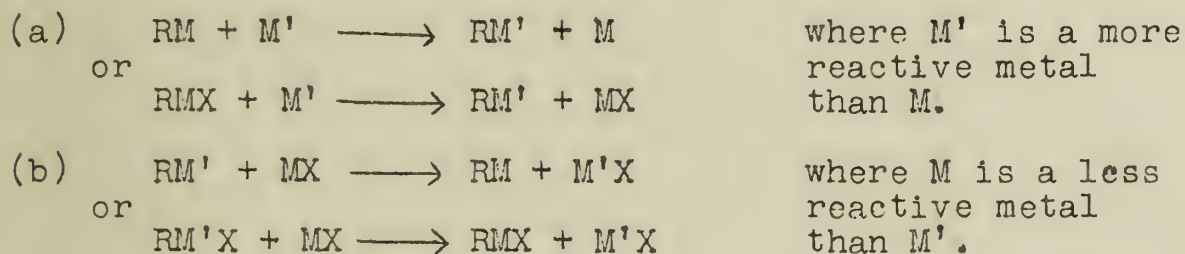
Diphenyl zinc reacts with benzonitrile, phenyl copper does not. Phenyl copper reacts with benzaldehyde, diphenyl mercury does not. Thus the following order of reactivity is indicated.



On the basis of yields with acetyl chloride and allyl bromide RCu is more reactive than is RAg. The RAu compounds are so unstable that they are placed at the end of the list.

This order of arrangement is rather broad and only holds when the R group connected to all of the metals in question is the same. For example, caesium phenyl is much more reactive than lithium phenyl, but lithium phenyl is more reactive than phenylacetylenyl caesium. Also as a general rule the alkyl organo-metallic compounds are more reactive than the aryl-organo metallic compounds.

General methods of preparing any of the organo-metallic compounds are as follows:



Suggested uses of some of the organo-metallic compounds.

The most reactive of the alkali metal organo-metallic compounds are good metalating agents. The metalated compound can then be carbonated to the acid. The aryl lithium compounds can be carbonated to give good yields of symmetrical ketones. The organo-cadmium compounds were found to be superior to organo-zinc compounds for the synthesis of ketones from acid chlorides. The organo-copper compounds were found to decompose smoothly to form R-R type hydrocarbons.

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THE CHEMISTRY AND STRUCTURE OF BORON HYDRIDES

Investigators: Stock) Chem. Inst. d. Tech.
 Wiberg) Hochschule, Karlsruhe
 Schlesinger - University of Chicago

For Bibliography see Wiberg, Ber., 69, 2816 (1936)

Since the discovery of boron hydrides they have created a great deal of theoretical interest since in them lies the possibility for single electron bonds.

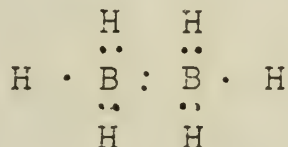
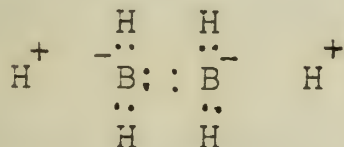
The six boron hydrides known today fall into two classes having the compositions B_nH_{n+4} and B_nH_{n+6} . They decompose more or less spontaneously, and are hygroscopic, being hydrolyzed by water to boric acid and hydrogen.

Boron hydrides were first prepared by Stock in 1912 by the hydrolysis of Mg_3B_2 , the principal product being B_4H_{10} . However, the yield for this reaction is very poor and made early work in this field exceedingly difficult. In 1931 Schlesinger and Burg found that B_2H_6 could be prepared in fair yield by subjecting a mixture of BCl_3 and H_2 to an electric discharge while under diminished pressure. Inasmuch as B_2H_6 and B_4H_{10} are the products obtained directly from the above reactions most of the experimental work on boron hydrides deals with them. In the last year or two better methods for the preparation of the higher boranes by heating these lower members have been developed, but as yet only a preliminary investigation of these hydrides has been carried out.

Although many structures have been proposed for the simplest boron hydride B_2H_6 , only two warrant much consideration, namely, that of Wiberg (I), and that of Sidgwick and Pauling (II).

I.

II.



The first compares diborane to ethylene in accordance with the theory of Grimm, whereas the second relates diborane to ethane. Using Grimm's idea O_2 , C_2H_4 , and B_2H_6 are put into a single class inasmuch as each system has 12 valence electrons. On this same basis ethane would be compared with $B_2H_6^{++}$ and $N_2H_6^{++}$. Actually $B_2H_6^{--}$, as in $B_2H_6K_2$, is much stabler than is diborane.

Physical measurements such as the parachor, magnetism, and dipole moment favor Wiberg's formula, and furthermore the diborane absorption in the ultraviolet is almost identical with that of ethylene, whereas ethane does not absorb in this region.

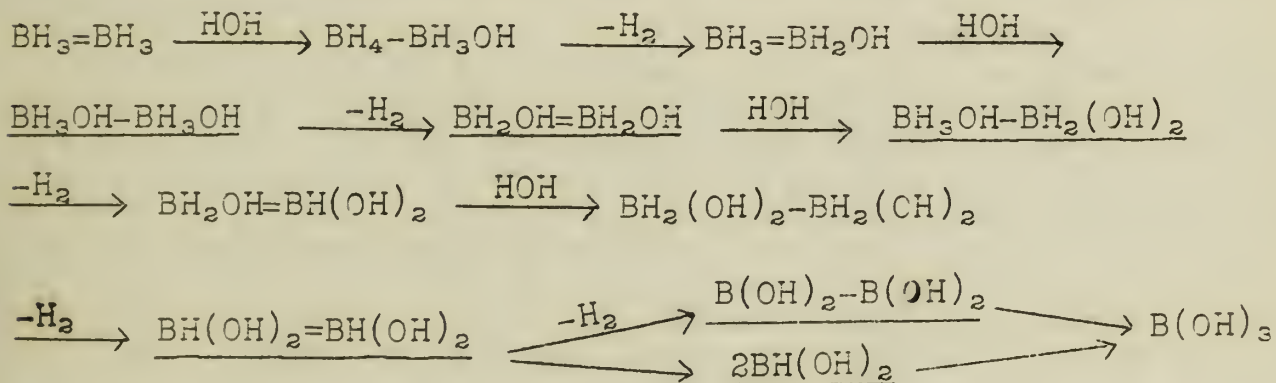
Wiberg proposes for B_4H_{10} a butadiene-like structure since it can be made from B_2H_5I by a Würtz reaction. From electron diffraction work Pauling has concluded that B_5H_9 contains a 4-membered boron ring. It seems likely that B_6H_{10} and $B_{10}H_{14}$ might contain this same ring.

The reactions of B_2H_6 and B_4H_{10} illustrating their acidic and unsaturated nature may be summarized as follows:

	B_2H_6	B_4H_{10}
Salt with NH_3 <u>A</u>	$B_2H_4(NH_4)_2$	$B_4H_6(NH_4)_4$
Product obtained by electrolizing A in liquid NH_3	$B_2H_2(NH_2)_2H_2$	$B_4(NH_2)_6H_4$
Product obtained by heating A	$B_3N_3H_6$	$B_3N_3H_6$
Salt with $K(Hg)_x$	$B_2H_6K_2$	$B_4H_{10}K_2$
Reaction with HCl	B_2H_5Cl	
Reaction with BCl_3	B_2H_5Cl	
Reaction with XS $B(CH_3)_3$	$B_2(CH_3)_4H_2$	

The compound $B_3N_3H_6$ is a cyclic, benzene-like compound.

The hydrolysis of B_2H_6 has been postulated as follows:



Derivatives of the underscored compounds have been isolated and analyzed.

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HYDROGENATION OF PYRROLES

F. K. Signaigo and H. Adkins, University of Wisconsin

Previous work: High pressure hydrogenation of esters.

Pyrroles have been found to be one of the unsaturated systems most resistant to hydrogenation. By the use of CuCrO or Raney nickel catalysts and hydrogen pressures from 70 to 350 atms., the greater number being between 200 and 300 atms., it has been possible to obtain pyrrolidines or substituted pyrrolidines and pyrroles in much better yields than was formerly possible. The way is also opened for the synthesis of a number of these compounds not previously prepared.

The hydrogenation of pyrroles carrying no N-substituent yielded about 50 per cent of the pyrrolidine. Forcing the reduction to completion still yielded about 50 per cent of the pyrrolidine and high boiling residues.

In contrast, the N-substituted pyrroles were readily reduced by the use of Raney nickel at temperatures from room temperature to 160°. (I) None of the acyl or carbalkoxy pyrroles unsubstituted on the N could be hydrogenated under conditions which did not reduce the acyl or carbalkoxy groups also.

Acyl groups in positions 2,3,4, or 5 are more readily reduced than the ring and the reduction may be interrupted to prepare the corresponding alkyl derivatives in good yields. However, the 2- and 5-positions are more readily reduced than the 3- and 4-positions and these former may be selectively reduced. (II) In the hydrogenation of the acyl-pyrroles there was no hydrogenation of the ring below 180°.

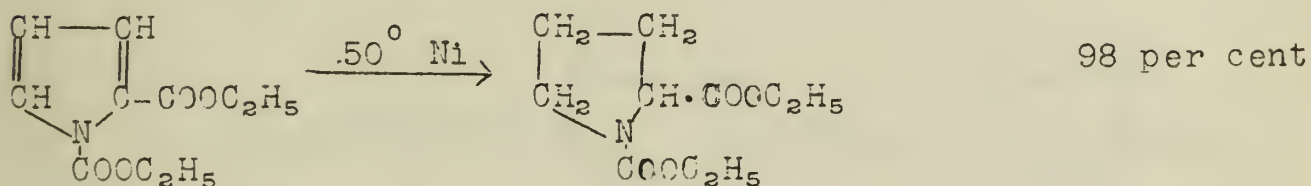
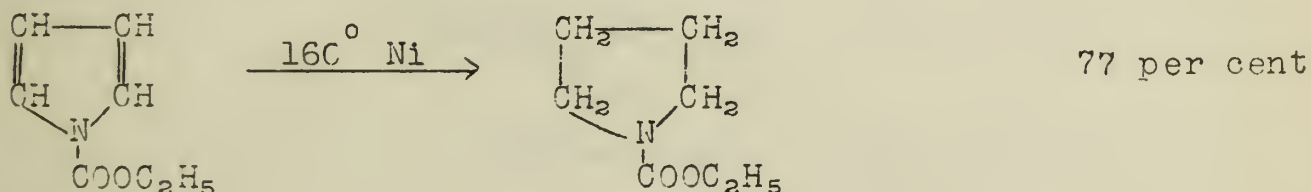
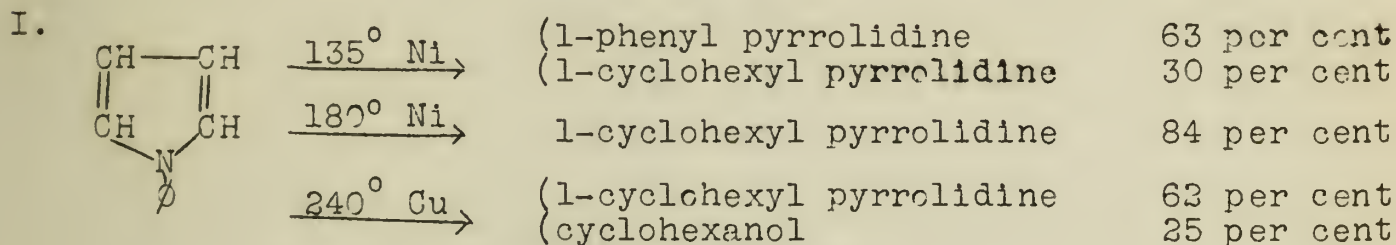
Carbethoxy groups in positions 2,3,4, or 5 require a higher temperature for reduction to a methyl group than the acyl groups require. (III) In fact the temperature required for the formation of the methyl pyrrole is within the range for the hydrogenation of the pyrrole nucleus. Therefore, the reaction must be interrupted at an intermediate stage to obtain a maximum yield of the substituted pyrroles. As with the acyl pyrroles a difference in the ease of hydrogenolysis of the 2- and 3-carbethoxy pyrroles is found, the former undergoing hydrogenolysis more readily, as is illustrated by the fact that a 2-carbethoxy pyrrole yields 30-50 per cent of the 2-methyl pyrrole, while a 3-carbethoxy pyrrole yields 0-10 per cent of the 3-methyl.

If CuCrO is used with temperatures of 200-250° the pyrrole nucleus is also reduced, but the ethyl alcohol which forms reacts with the pyrrolidine to give an N-ethyl pyrrolidine. This alkylation of the pyrrolidine N may be avoided by using a tert-butyl ester in dioxane, which upon hydrogenolysis gives the methyl group, tert-butyl alcohol and water.

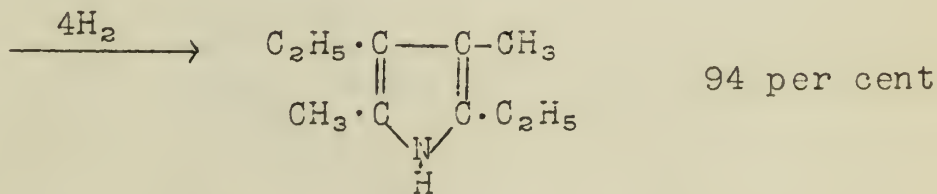
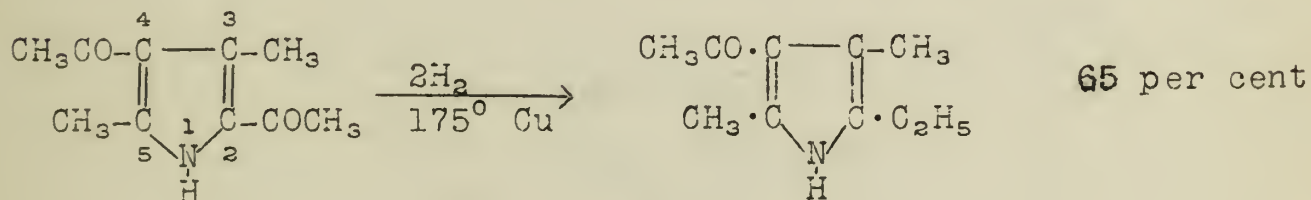
The 1,2-dicarbethoxy pyrrolidine was hydrogenated for comparison, (IV) the two alcohols (a and c) being isolated as intermediate products; (b) could not be isolated.

Attempts to stop the hydrogenation of acyl pyrroles at the carbinol stage were unsuccessful. However, this object may be achieved with aryl aldehydes and ketones and no difficulty is encountered in stopping the reduction of furfuraldehyde at the carbinol stage.

A practical synthesis of dl-Proline is possible through the hydrogenation of 1,2-dicarbethoxypyrrole. Over all yields from pyrrole are 55-60 per cent.

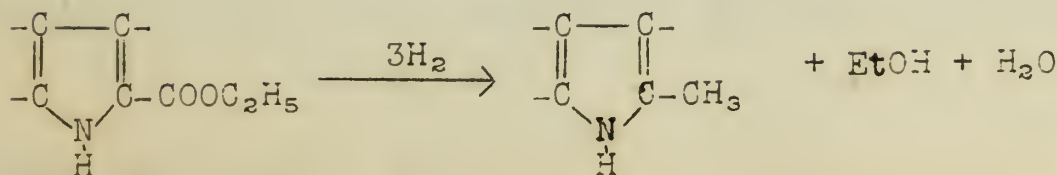


II.



Above 180° red'n. to the pyrrolidine occurs.

III.



THE SYNTHESIS OF PYRROLIDINES, PIPERIDINES
AND HEXAHYDROAZEPINES.

J. H. Paden and Homer Adkins, University of Wisconsin
J. Am. Chem. Soc., 58, 2487 (1936)

Piperidines from Glutaramides.--Glutaramide gave a 70 per cent yield of piperidine by treatment with hydrogen under 200-400 atmospheres pressure over copper-chromium oxide at 250° in dioxane solution. Piperidines substituted in the 1 and 4 positions were obtained in similar yields from N-monosubstituted amides of glutaric and β -substituted glutaric acids (I). Di-N-pentamethylene glutaramides gave open-chain diamines--substituted cadoverines.

Pyrrolidones and Piperidones from Imides.--Succin- and glutarimides which bear an alkyl group on the nitrogen atom may be converted at 200-220° over Raney nickel to 2-pyrrolidones and 2-piperidones, respectively. In the hydrogenation of N-phenethylsuccinimide it was found possible to isolate 1- β -cyclohexylethylsuccinimide in a yield of 93 per cent (II).

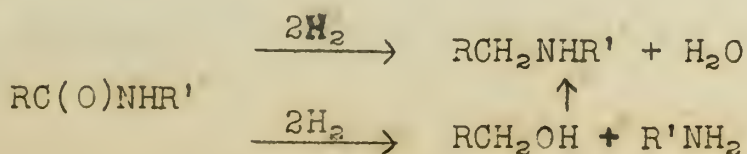
Piperidines from Glutarimides.--Even though the piperidine ring system is already present in a glutarimide, the yields of piperidines from glutarimides are of the same order of magnitude as from glutaramides under the same conditions. The hydrogenation of N-unsubstituted glutarimides was not very satisfactory.

Pyrrolidines and Piperidines from Pyrrolidones and Piperidones.--Two 2-pyrrolidones and one 2-piperidone have been converted over copper-chromium oxide to the corresponding pyrrolidines and piperidine in yields of 88-96 per cent.

Pyrrolidines and Piperidines from Glycols and Amines.--It seemed possible that the cyclic amines were formed from glycols and amines produced by the hydrogenolysis of the carbon to nitrogen bond in the amides. Examination of this possibility led to another method for preparing cyclic amines. Primary amines were found to react with 1,4- or 1,5-glycols under the conditions used for the hydrogenation of amides, to give 68-77 per cent yields of pyrrolidines or piperidines (III).

Hexahydroazepines.--The hydrogenation of di-N-n-amyladipamide over copper-chromium oxide gave a 45 per cent yield of 1-n-amylhexahydroazepine and 41 per cent di-n-amylamine. Treatment of hexanediol-1,6 with benzylamine gave a 23 per cent yield of 1-benzylhexahydroazepine which was converted to hexahydroazepine by treatment with hydrogen over copper-chromium oxide at 275° (IV).

Mechanism of Conversion of Amides to Cyclic Amines.--The conversion of an amide to an amine of the same carbon content may take place in two ways neither of which is definitely ruled out by experimental observations.



Volume 1, Number 1, Spring 1964

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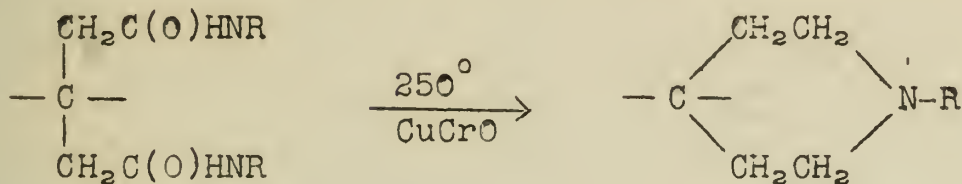
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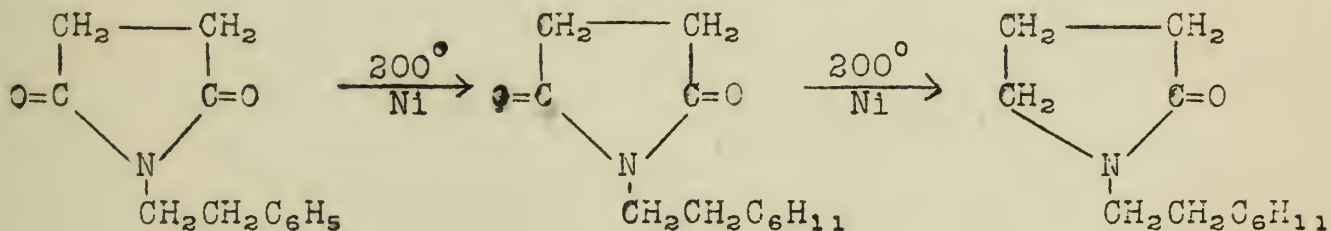
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Insofar as the formation of cyclic amines from open-chain amides is concerned, it appears that hydrogenation precedes ring closure.

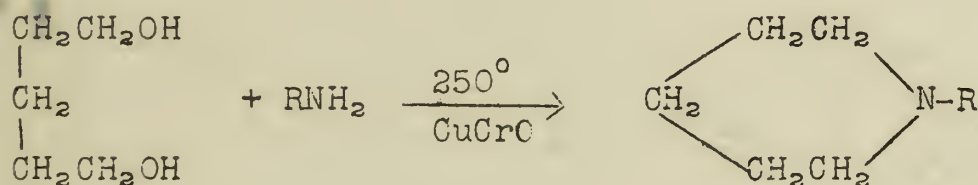
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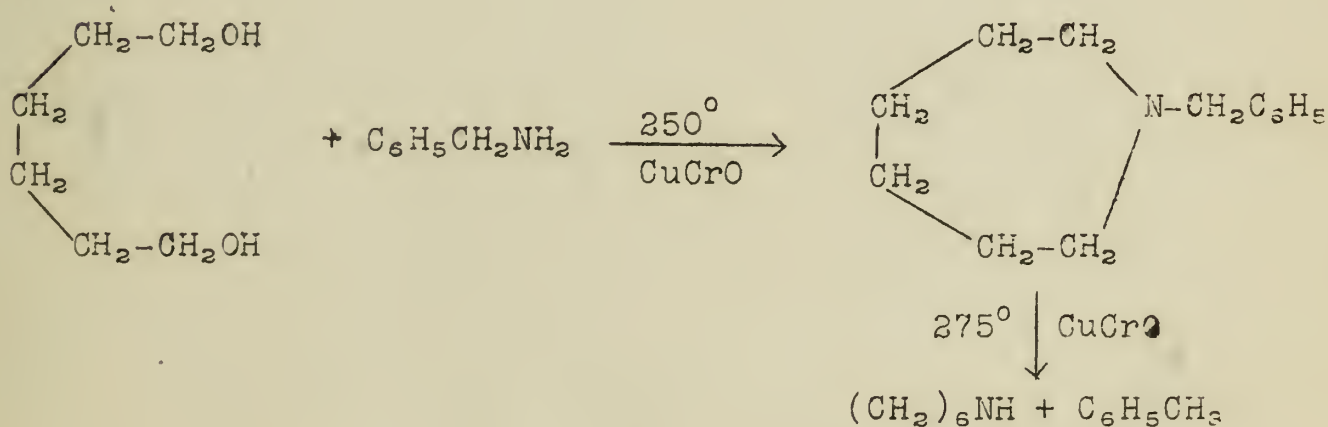
II.



III.



IV.



1. The first part of the report is a general statement of the purpose of the study and the scope of the work.

1941

SEMINAR TOPICS

II Semester 1936-37

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PROGRESS IN CHEMISTRY AND STEREOCHEMISTRY OF DEUTERIUM

I. Chemistry

(A) Source.--The mixture of 200,000 parts of deuterium, D, and 1 part of tritium, T, per billion of protium, commonly called hydrogen, can be partially separated into its components by making use of any property in which the components differ. The methods which have been found practically applicable are electrolysis, distillation, desorption from charcoal, and diffusion through palladium. The only method used technically is the fractional electrolysis of water, presumably between nickel electrodes in basic solution and this has been developed to a high degree of efficiency.

(B) Methods of Introduction.--In preparing organic compounds containing deuterium, many different reactions have been utilized, for example:

1. Reduction of double and triple bonds
2. Exchange for an active hydrogen
3. Decomposition of a Grignard with D_2O
4. Polymerization of C_2D_2 to C_6D_6
5. Decomposition of Ca salts with $Ca(OD)_2$
6. Acidification of salts with DCl
7. Addition of D_2O to ketenes and acetylene
8. A Friedel-Crafts-like exchange of D for H.

(C) Properties.--Since the discovery of deuterium, great interest has centered in the effect of substitution of D for H on physical constants.

1. Density is invariably increased. A close approximation is made by assuming the atomic volumes of D and H the same:

$$d_D = d_H \left[1 + \frac{N_D(1.006)}{M} \right]$$

N_D = number of D atoms

M = mol. wt. of H compound

	H		D	
		Calc.		Found
Benzene	0.8736	0.9411		0.9417
Chloroform	1.4888	1.5013		1.5004
Diethylcarbinol	0.8204	0.8579		0.8538

2. Boiling point is variably affected.

	H		D
Benzene	80.1°		79.3°
Chloroform	61.2		61.7

3. Melting point generally lowered:

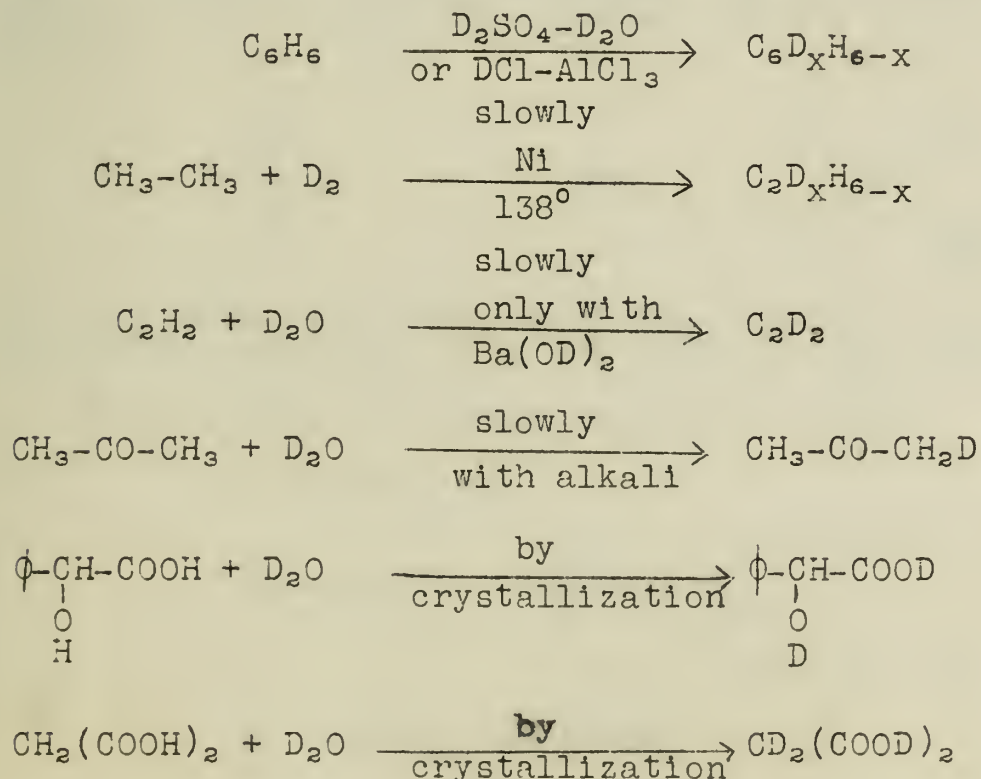
$CD_2(COOD)_2$	4°	lower than $CH_2(COOH)_2$
CD_3COOD	0.8°	lower than CH_3COOH
CH_3COOD	3.3°	lower than CH_3COOH
C_6D_6	1.3°	higher than C_6H_6

4. Refractive index affected slightly and unpredictably.

	H	D
Benzene	1.4998	1.4978
Dimethyl succinate	1.4198	1.4302
Diethylcarbinol	1.4103	1.4073

5. The frequency of the absorption band due to a hydrogen bond formed by deuterium differs from that formed by protium by a factor $\sqrt{2}$, which furnishes a valuable key to spectroscopic study of hydrogen bonds.

(D) Exchanges.--The ease of replacement of H by D depends upon the chemical activity of the H, and varies from practically instantaneous replacement of ionic H to the slow replacement of "inactive H," such as in benzene, which takes place only under the influence of a catalyst, for example:



The readiness of exchange in the latter cases has been made the basis of two methods of determining the number of "active H atoms" in a molecule. One⁸ depends on the gain in weight by replacement, the other⁹ depends upon analysis of the compound for relative abundance of the isotopes. The "active H number"

Baron, L. J. 1960. *Vol. 1* (1960) 1-100.

$$\begin{array}{rcl} \pi(8,00)_{\text{H}} & \text{H} & \pi(8,00)_{\text{H}} \\ \text{H} & \text{H} & \text{H} \\ \text{H} & \text{H} & \text{H} \\ \text{H} & \text{H} & \text{H} \end{array}$$

THE UNIVERSITY OF CHICAGO

1897

1. The first part of the document is a list of names and addresses, which are arranged in a columnar fashion. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list includes names such as "John Smith", "Mary Jones", and "Robert Brown", along with their respective addresses.

determined in this way may be larger than the Zerewitinoff number.

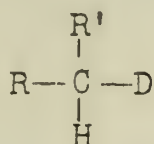
(E) Analysis.--Determination of per cent D resolves itself into determination of the D:H ratio in the water formed on combustion. Three methods are applicable:

1. Interferometer. Requires 1 g. of water and is insufficiently accurate in low D concentrations.
2. Determination of density by varying temperature till a "swimmer" of known density neither sinks nor floats.
3. Determination of density by varying pressure until a submerged float neither sinks nor rises.

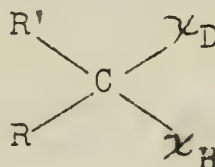
Either of the last two methods is sufficiently accurate to differentiate between, for example, $C_6H_4.995 D_{1.005}$ and $C_6H_5.005 D_{0.995}$ and thus are quite successful for isotopic analysis.

II. Stereochemistry

Since various differences in the properties of compounds have been noted where deuterium takes the place of protium, it has been a debatable question whether the difference between the two atoms is great enough to engender optical activity in molecules such as:



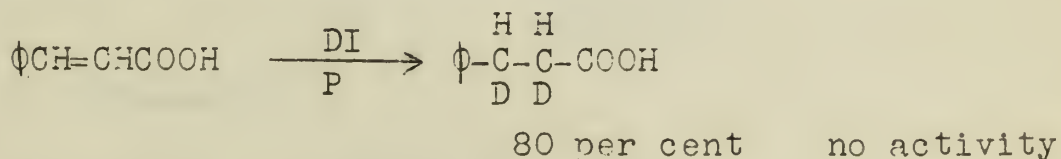
and



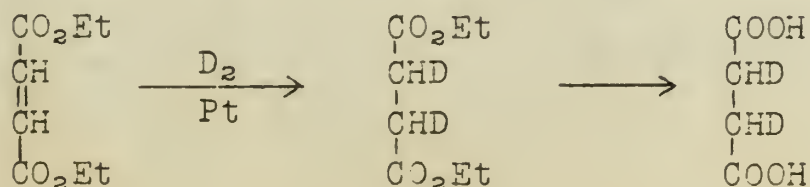
and, if there is optical activity, whether it is in any case, of sufficient magnitude to be detected in the ordinary polarimeter.

These studies have been reported to date:

1. Erlenmeyer¹



2. Leffler and Adams²



cis and trans

no activity

...in this way, ...to ...

...the ... of ...

...the ... of ...

...the ... of ...

...the ... of ...

...the ... of ...

...the ... of ...

...the ... of ...

...the ... of ...

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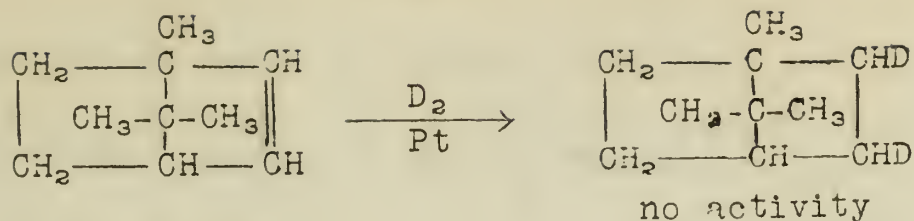
...the ... of ...

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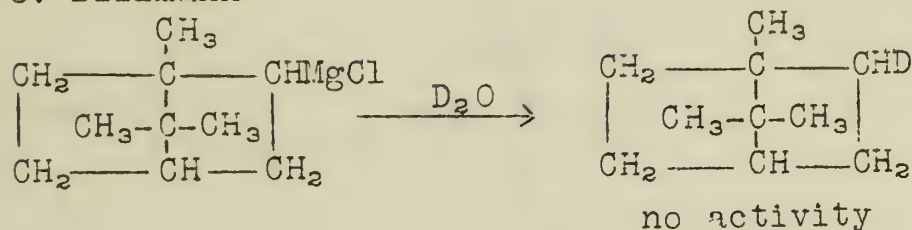
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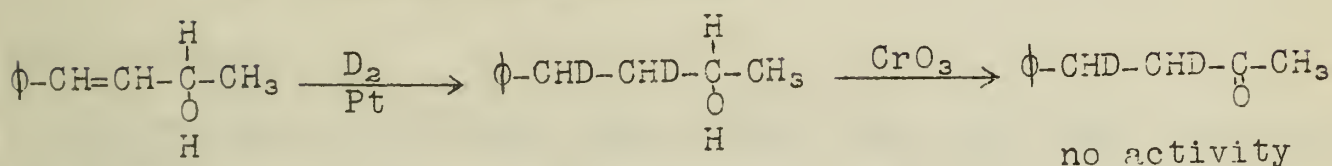
...the ... of ...



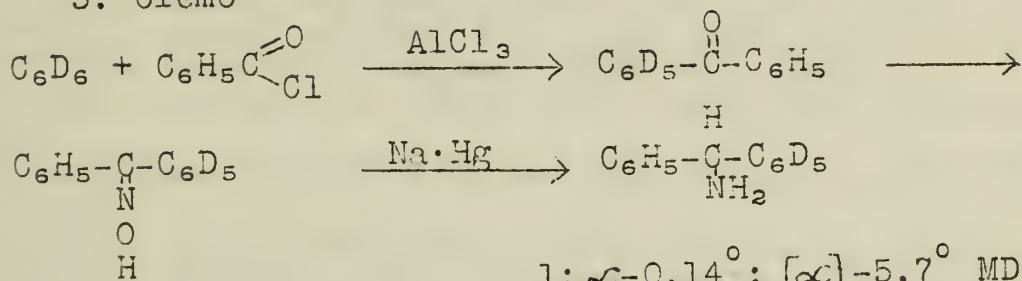
3. Biilmann³



4. Coppock and Partridge⁴

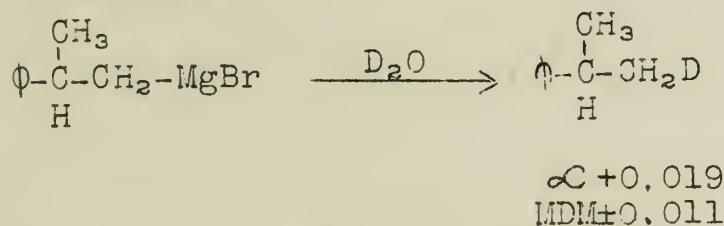


5. Clemo⁵

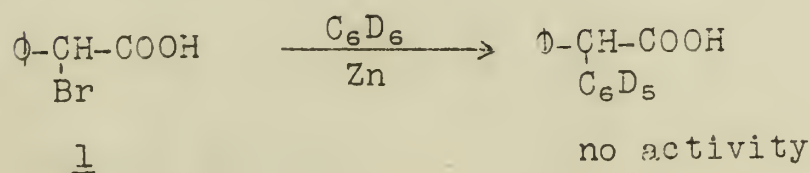


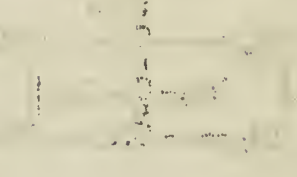
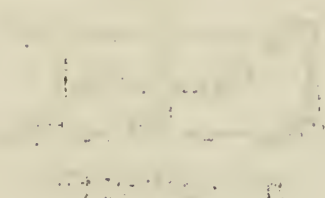
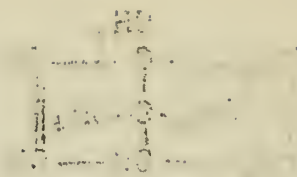
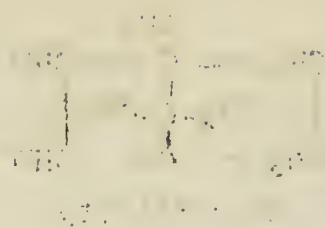
$$\begin{array}{l}
 \underline{l}: \infty - 0.14^\circ; [\infty] - 5.7^\circ \quad \text{MDM} \pm 0.010^\circ \\
 \underline{d}: \infty + 0.04^\circ; [\infty] + 5.0^\circ \quad \text{MDM} \pm 0.009^\circ
 \end{array}$$

6. Wallis⁶



7. Erlenmeyer⁷



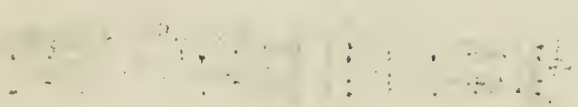


Reaction of 2,2,4,4-tetramethylpentane with bromine



The reaction of 2,2,4,4-tetramethylpentane with bromine yields 2-bromo-2,2,4,4-tetramethylpentane and hydrogen bromide.

The reaction is a free radical substitution reaction.

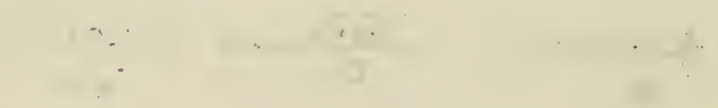


2,2,4,4-tetramethylpentane



2-bromo-2,2,4,4-tetramethylpentane

Hydrogen bromide

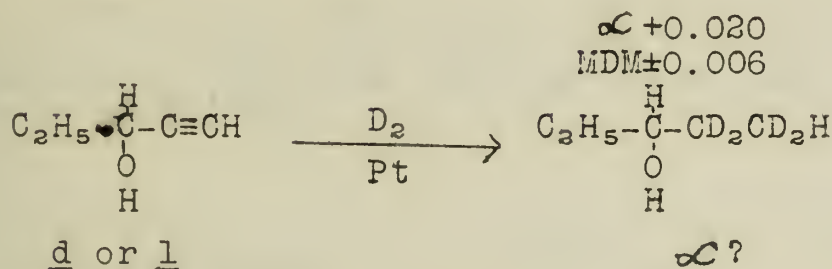
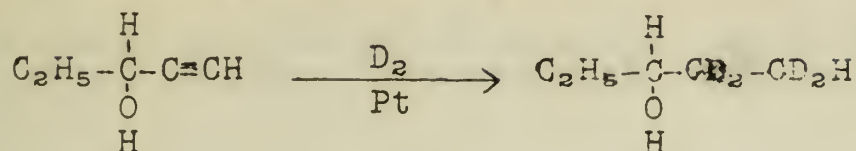


2,2,4,4-tetramethylpentane

Br₂

-5-

These reactions are now in progress here.



Bibliography:

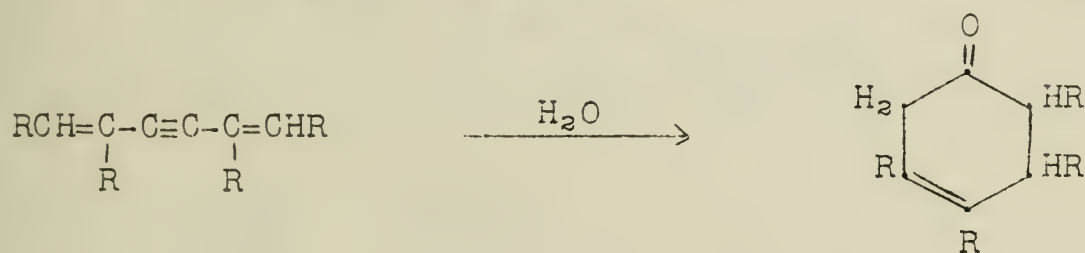
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3. Billmann, Jensen, and Knuth, *Ber.*, 69, 1031 (1936)
4. Billmann, Jensen, and Bak, *Ber.*, 69, 1947 (1936). Copenhagen.
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Reported by Frank C. McGrew
February 10, 1937.

HYDRATION AND CYCLIZATION OF SUBSTITUTED DIVINYLACETYLENES

A number of cyclization reactions which have been of greatest value in the synthesis of polynuclear compounds are shown in equations 1-10.

A study of the reactions of substituted divinylacetylenes carried out in this laboratory¹¹ has led to a new method for the preparation of ring from open-chain compounds. The general reaction is as follows:



This reaction has been used in the production of mono-,^{11,12} di- and tricyclic¹³ ring systems as illustrated by equations 11-13. The reagents used for hydration-cyclization were a cold solution of sulfuric acid in acetic acid or boiling 85 per cent formic acid. The yields obtained were 20 to 60 per cent.

Substituted divinylacetylenes were prepared from the corresponding acetylenic glycols by dehydration with 27 per cent sulfuric acid, 60 per cent phosphoric acid or potassium acid sulfate. It was possible to carry out the dehydration and hydration-cyclization in one operation with the cyclizing reagents mentioned above, but there were more side reactions than in the two-step process.

Symmetrical acetylenic glycols were prepared by treating the dimagnesium halide of acetylene with the appropriate ketones. Unsymmetrical glycols were prepared from 1-ethynylcyclohexanol. This acetylenic alcohol was treated with an excess of ethylmagnesium bromide and then with the appropriate ketones.

The cyclic nature of the product in equation 11 was proved by ozonization to the known α,β -dimethyl- γ -ketovaleric acid, dehydrogenation to 2,3,4,5-tetramethyl phenol and reduction to hexahydroprehnitene which gave prehnitene by dehydrogenation.

The product in equation 13 was reduced stepwise with zinc amalgam and hydrochloric acid, and hydrogen at 250° and 2000 lbs. pressure over Raney nickel to a saturated hydrocarbon, the physical properties of which agreed with those of perhydrophenanthrene prepared by the hydrogenation of phenanthrene, and were quite different from those of 1,2-dicyclohexylethane.

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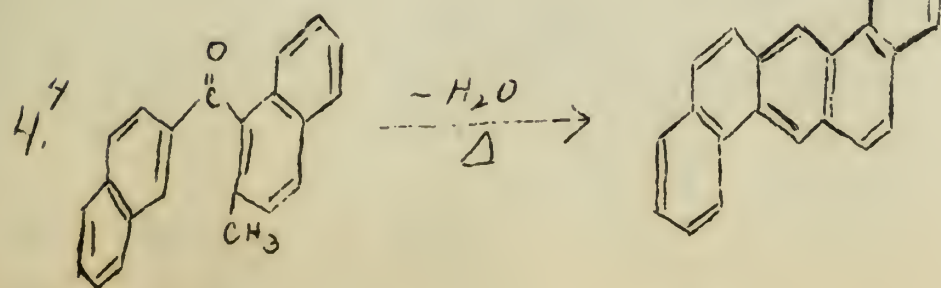
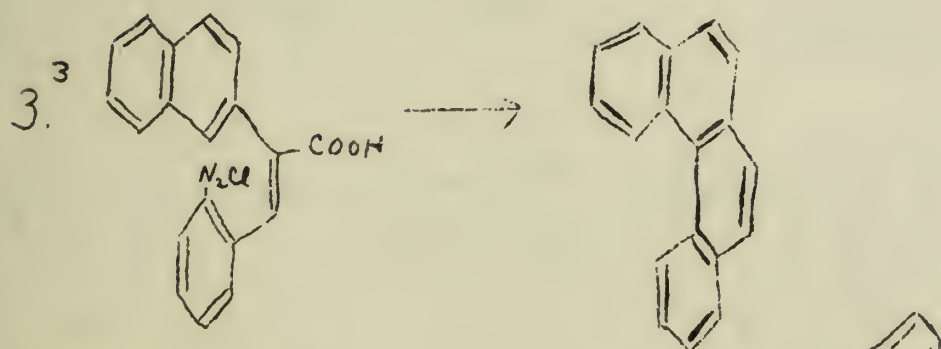
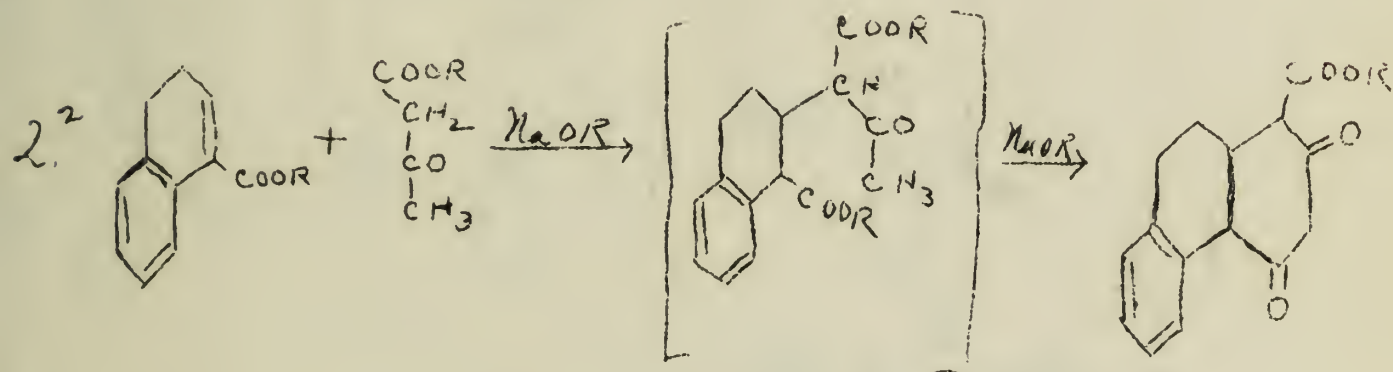
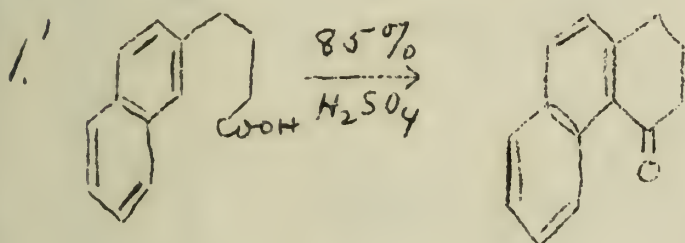
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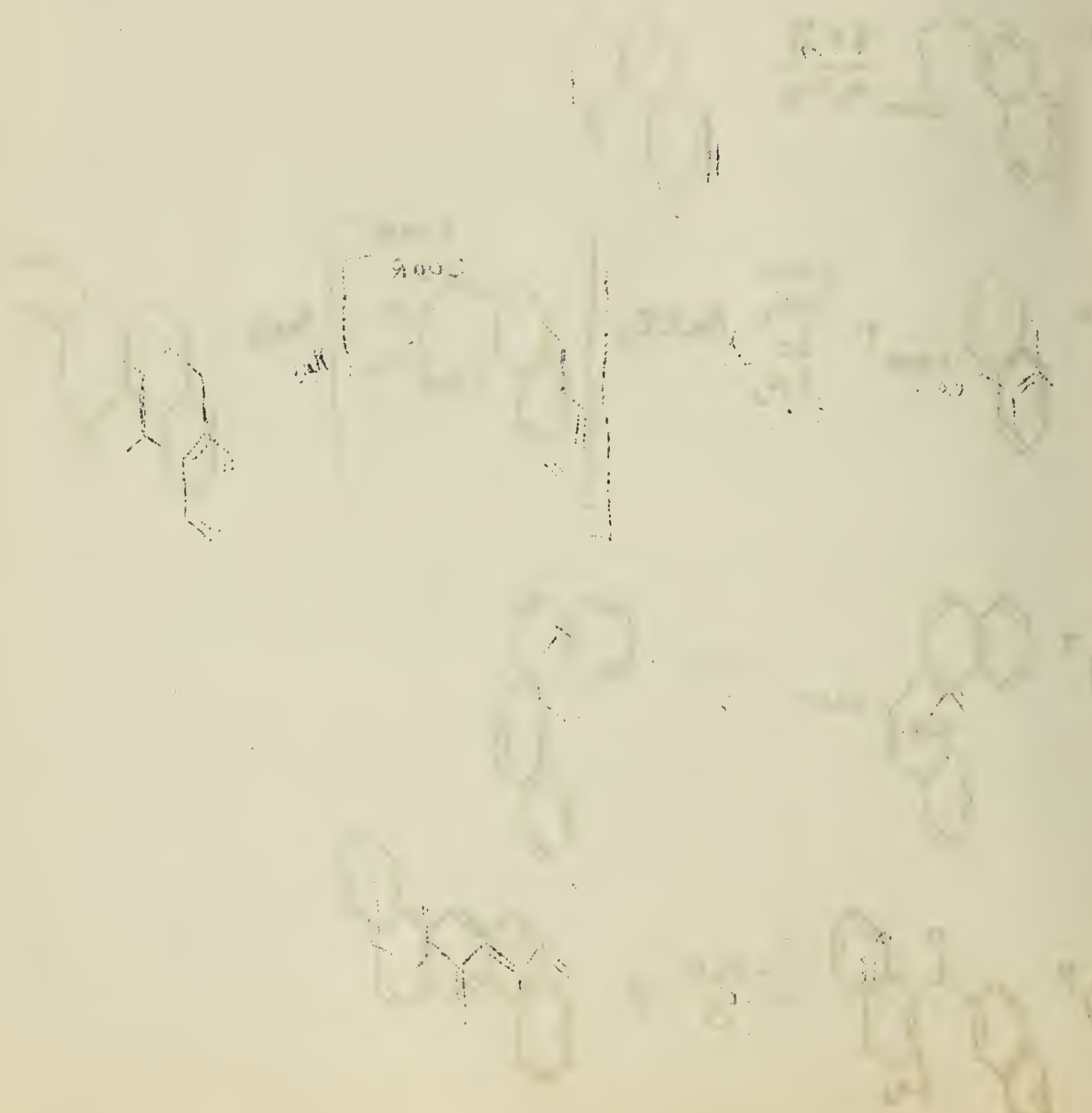
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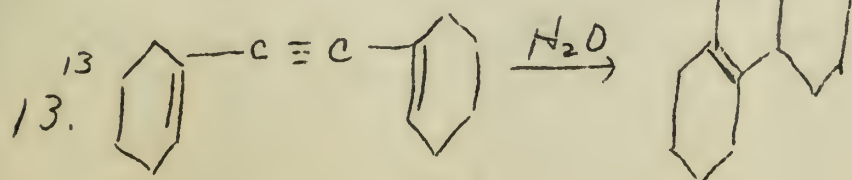
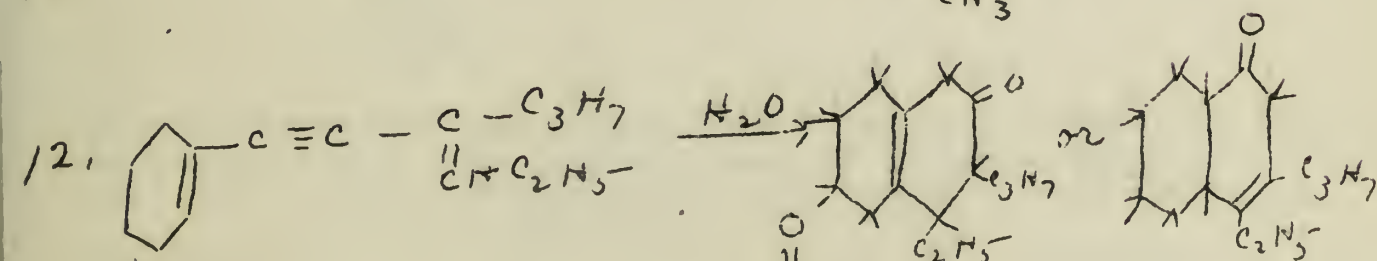
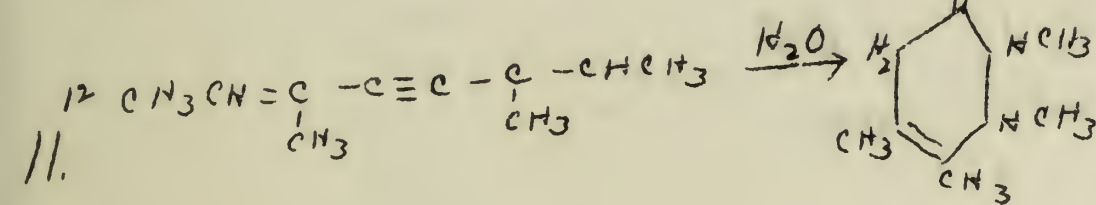
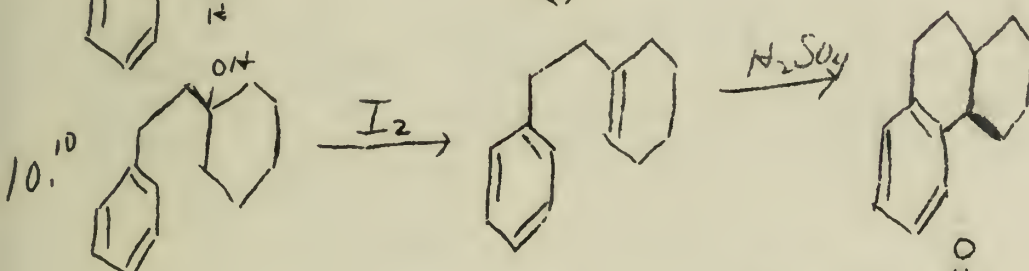
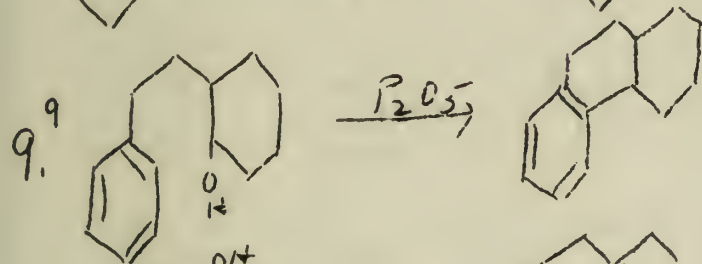
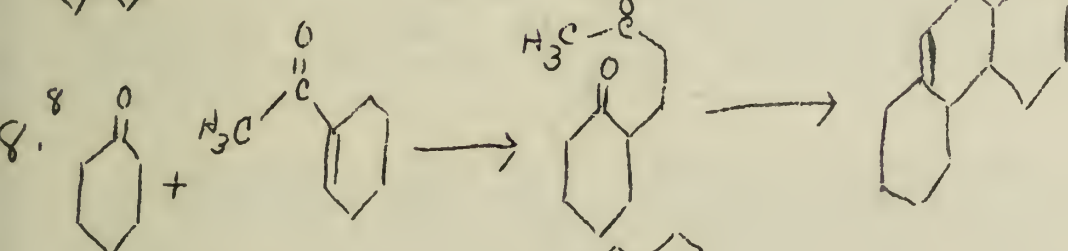
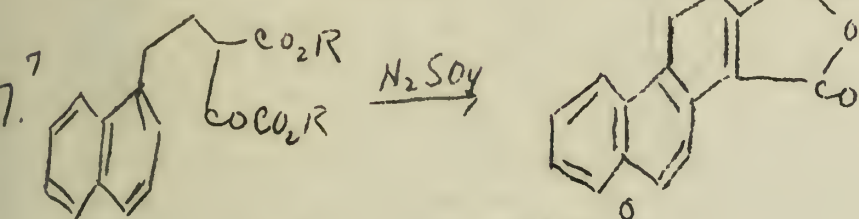
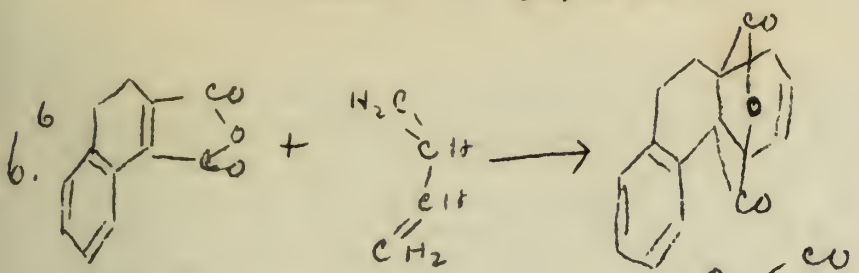
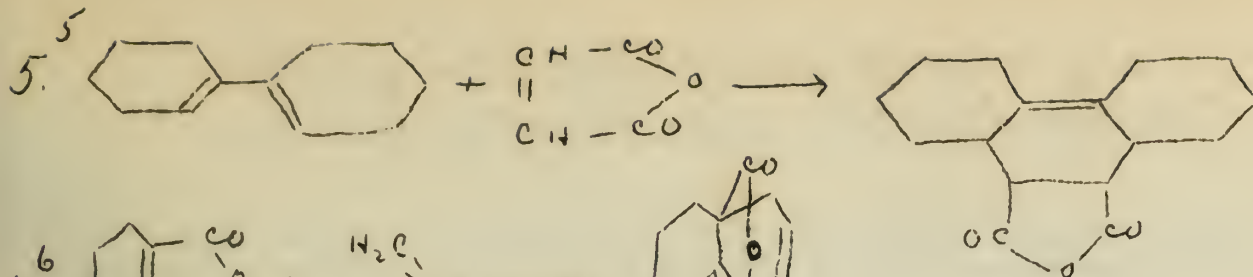
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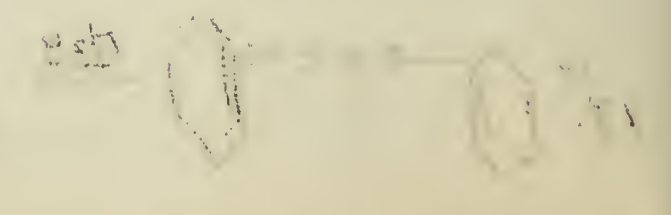
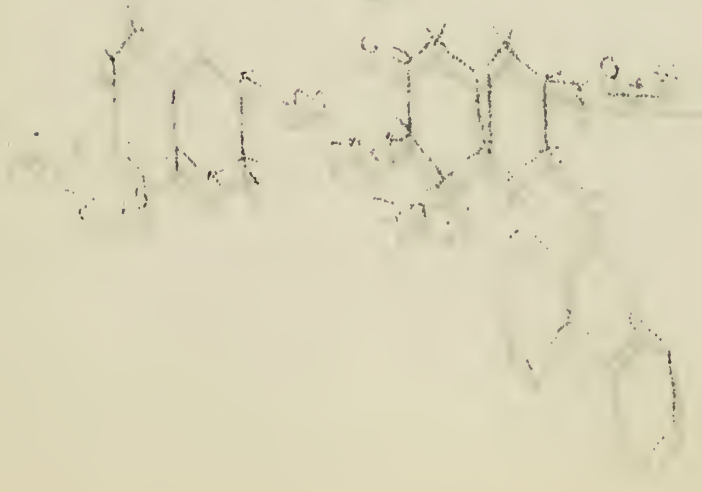
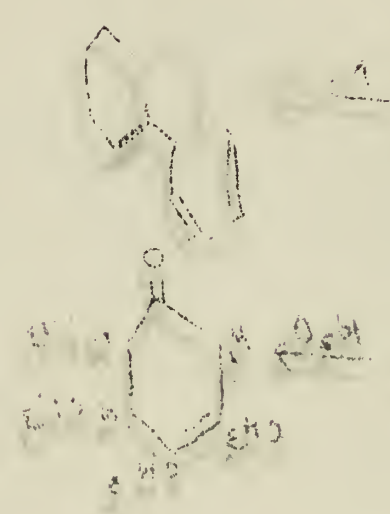
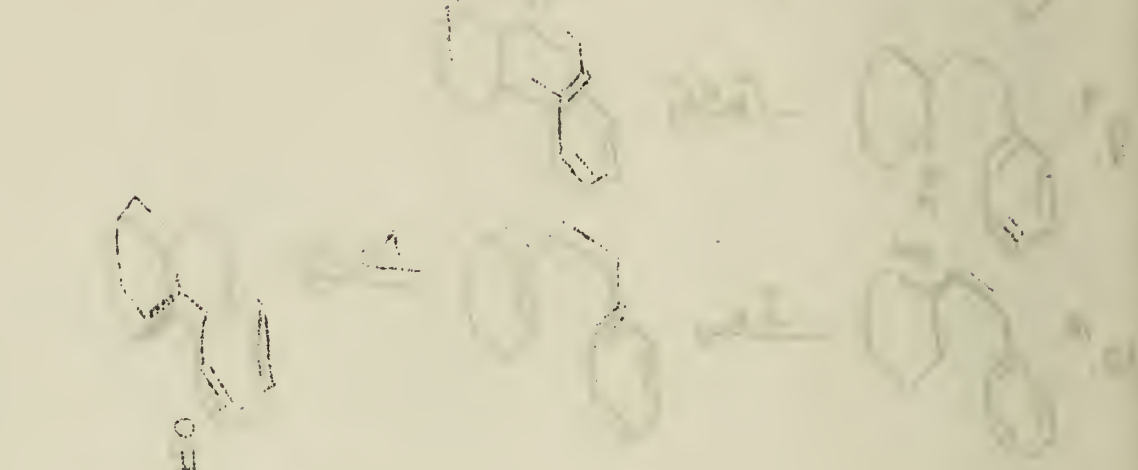
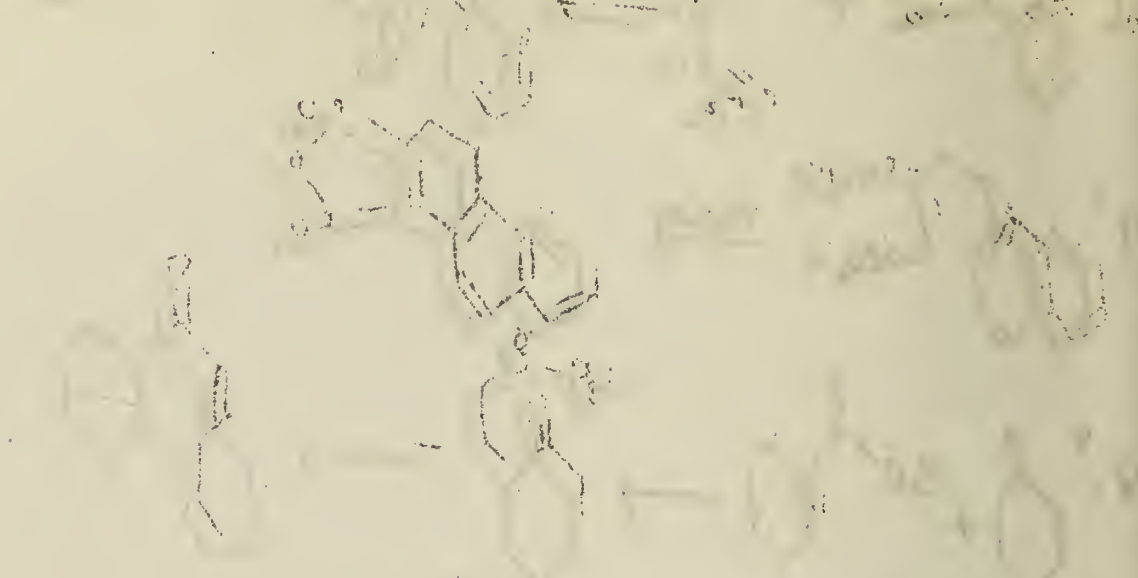
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13. Pinkney, Nesty, Wiley and Marvel, *ibid.*, 58, 972 (1936).



1. The first part of the report is a general introduction to the subject of the study. It discusses the importance of the problem and the objectives of the research. The second part of the report is a detailed description of the experimental methods used. This includes a description of the apparatus, the materials used, and the procedures followed. The third part of the report is a discussion of the results of the experiments. This includes a description of the data obtained, a comparison of the results with previous work, and a discussion of the implications of the findings. The fourth part of the report is a conclusion, which summarizes the main findings of the study and suggests directions for future research.





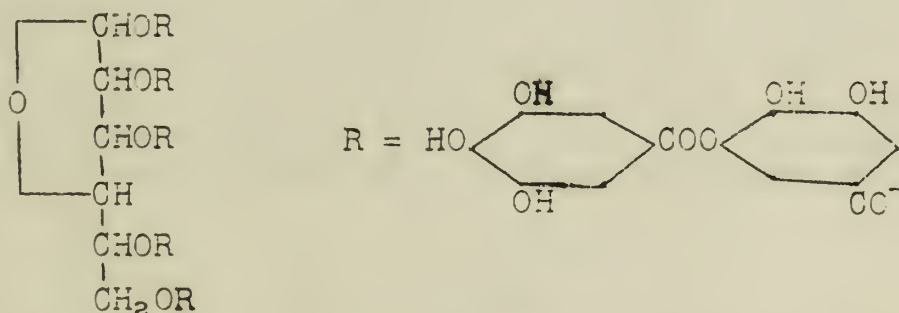


METHODS FOR DETERMINING STRUCTURES OF HIGH MOLECULAR WEIGHT NATURALLY-OCCURRING SUBSTANCES

The increased complexity of the naturally-occurring high molecular weight substances necessitates a somewhat different approach to the problem of determining their structure. Difficulties of isolation, purification, and crystallization have also caused trouble, especially by confusing the early literature with apparently contradictory results. The general method of breakdown and synthesis is at the root of all structure determinations. However, in most cases the method of linking the breakdown products together is equally, if not more, important than the actual structural units involved. In some cases, activity is dependent upon the molecule as a whole, so that breakdown destroys the effectiveness of the substance. In physiological work, this vitiates the breakdown approach. We shall consider four classes: tannins, cellulose and starch, lignins, and certain physiologically specific groups.

Tannins.--This class covers a large range of naturally-occurring compounds that are not necessarily structurally related and are widely distributed. Their common characteristic is the ability to precipitate proteins from aqueous solutions. Russell advises the use of three classes of tannins, distinguished by products of hydrolysis. The first class is composed of tannins related to depsides, which are derived from *p*-benzoyl oxybenzoic

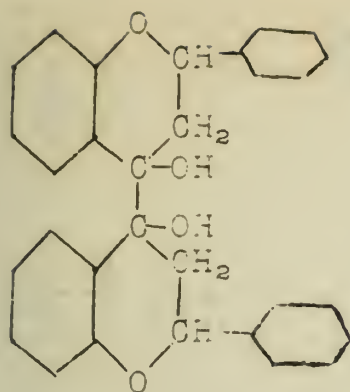
acid, $\phi\overset{\text{O}}{\parallel}\text{C}-\text{O}-\langle\rangle-\text{COOH}$. Gallotannin is the only naturally-occurring member of this class. Hydrolysis gives one molecule of glucose and ten molecules of gallic acid. The only formula which seemed logical from these results was the following; penta-m-digalloyl- β -glucose.



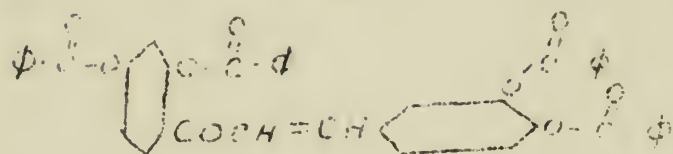
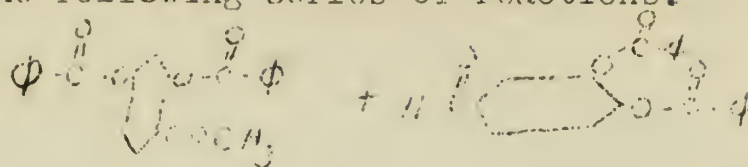
This compound was synthesized and found to be identical with the natural product. The second class of tannins, which give ellogic acid and glucose on hydrolysis, are those related to diphenyl-

dimethyloid, $\langle\rangle-\text{COO}-\langle\rangle-\text{O}-\text{CO}-\langle\rangle$. The structures of these

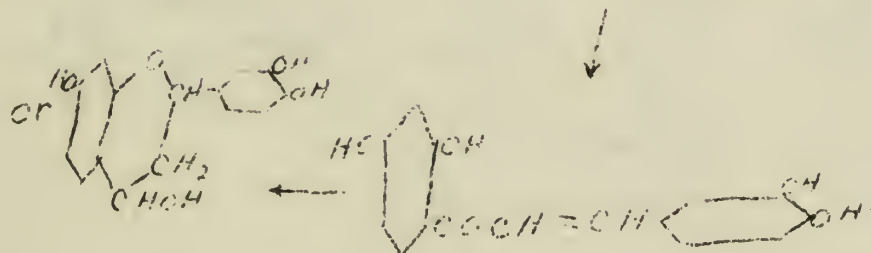
compounds have not been worked out well, and they are not numerous enough to warrant consideration. The third or phlobaphene-producing tannins, give phlobaphenes on hydrolysis and are known as phlobatannin. These represent the most abundant source of tannins. In contradiction to a proposed formula of Freudenberg, Russell proved this class to be phenolic hydroxy derivatives of flavinacol,



, by the following series of reactions.



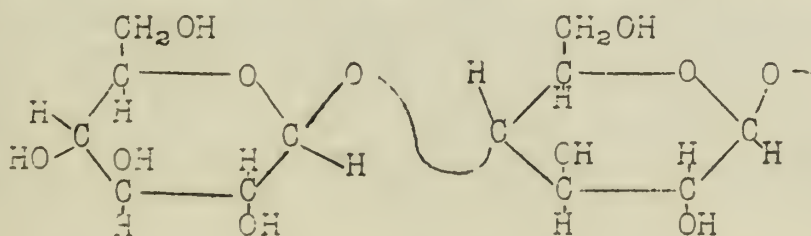
2,4,3',4'-tetrahydroxychalcone



2,4,3',4'-trihydroxychalcone

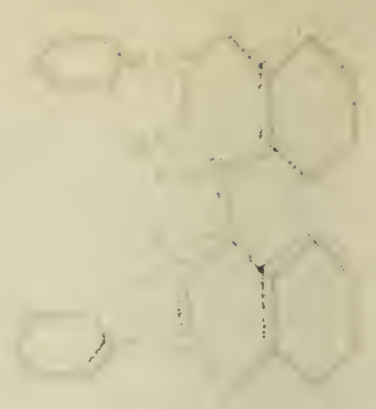
bis(7,3',4'-trihydroxy)flavoprenol

Cellulose.--Whereas it was essentially a matter of functional groups and the presence or absence of a dimer in the case of phlobatannins, the main question in regard to cellulose is inter-unit linkage. The hydrolytic breakdown product from cellulose is glucose. Glucose is also obtained from starch and glycogen. Hence, here our interest lies in the inter-unit linkages involved. Cellulose has been shown to be a polymer of β -glucose, with a



molecular weight of approximately 100-200 of these glucose units. Kuhn has developed a system of reaction kinetics which points to the presence of a homogeneous chain linked only with cellobiose units. The best confirmation of this type of linkage is found in a study of the optical rotatory power of the biose, triose, and tetraose compounds. This shows that the change in rotation observed between each of the above types is equal to the molecular rotation of the glucose units in the polysaccharides. The following series of reactions represent the proof of the structures of cellobiose.

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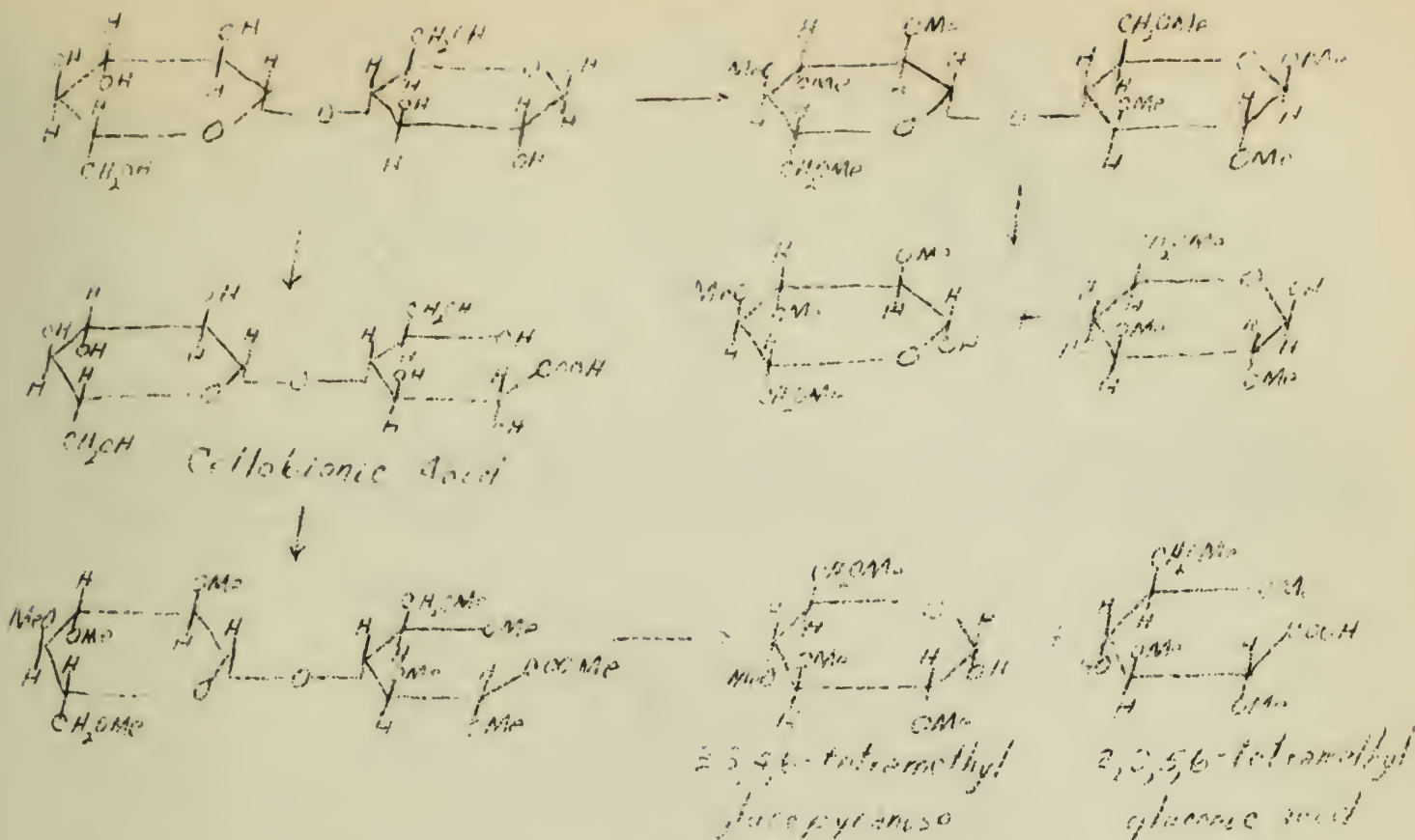
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Work on starch has followed the same general plan, but the starch molecule seems to be slightly more complicated than that of cellulose. A large difference in molecular weight is, of course, noted.

The lignin field is badly overrun by work which is purely descriptive in context and which deals with extractions, fractionations, analyses and molecular weight determinations of undefined fractions.

There appears to be two well defined methods of attack, the first of which treats lignin as a molecularly dispersed substance. Color reactions, molecular weight determinations and analyses, supplemented by methoxyl and hydroxyl determinations, enables one to write an empirical formula of $C_{46}H_{32}O_6(OCH_3)_5(OH)_5$ which means very little as far as the structure of lignin is concerned. Oxidations all go too far, yielding oxallic, adipic and succinic acids. Zinc dust distillation yields two important substances, namely anisic acid and 1-propyl-3-methoxy-4-hydroxy benzene.

The second method of approach considers lignin, with certain reservations, as a polymeric substance composed of some definite building unit which is a degradation product of the entire molecule, not a definite, self existing molecule as the former method indicates.

According to Freudenberg, the fundamental unit is predominately an oxymethoxyphenyl propane derivative (I). There probably occurs in addition some of the isovanallin type (II) as well as the piperonals (III).

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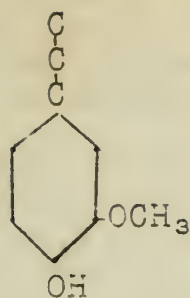
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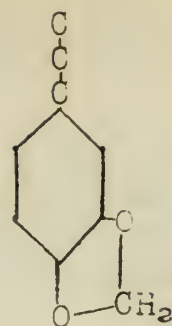
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I.

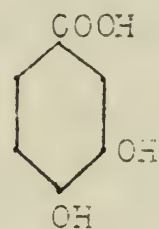
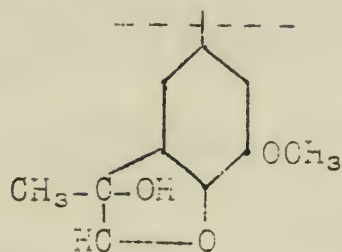
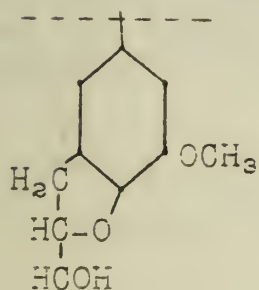
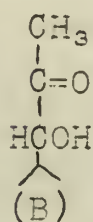
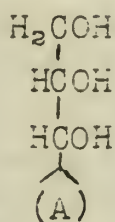


II.

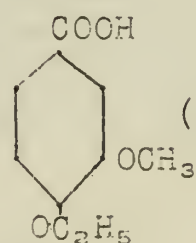
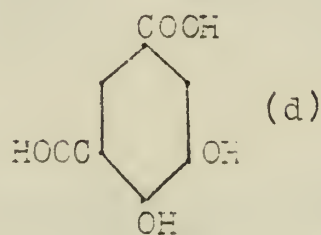
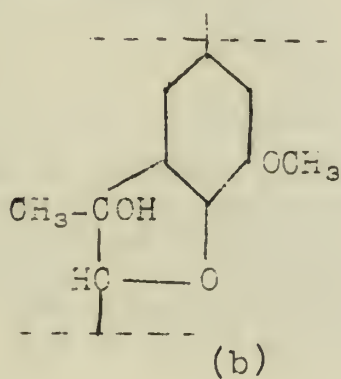
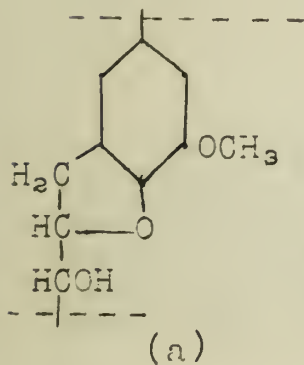


III.

The propane side-chain may have various configurations, the three most common being (A), (B) and (C) types. Likewise the method of union appears to vary, e.g., AI forms (a) while BI forms (b), etc.



(c) Protocatecholic acid



(e) ethoxy vanillic acid

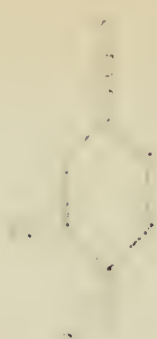
Experimental work of this second method of approach consists of determining the number of oxygen bridges that change to a methoxyl, the number of secondary and testing hydroxyls in (a) or (b) and most important of all identification of degradation pieces such as (c), (d) and (e). Nitration and bromination has revealed that 3 H atoms per lignin unit can be substituted.

One point must constantly be kept in mind in the lignin problem, namely that each fraction under investigation is a mixture of similar portions of different molecular size.

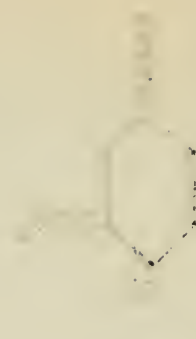
Another group of high molecular weight natural products that requires special methods are those substances having a specific



(10)



(11)

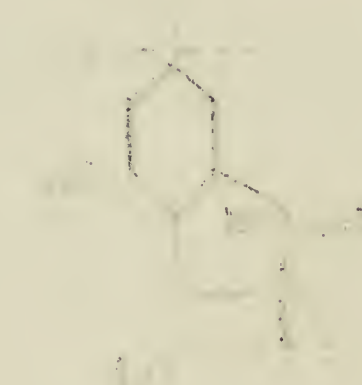


(12)

These three structures are examples of the general class of compounds which may be formed by the reaction of a benzene ring with a substituent group. The structures are shown in the form of a chemical equation, with the reactants on the left and the products on the right. The structures are labeled (10), (11), and (12) respectively.



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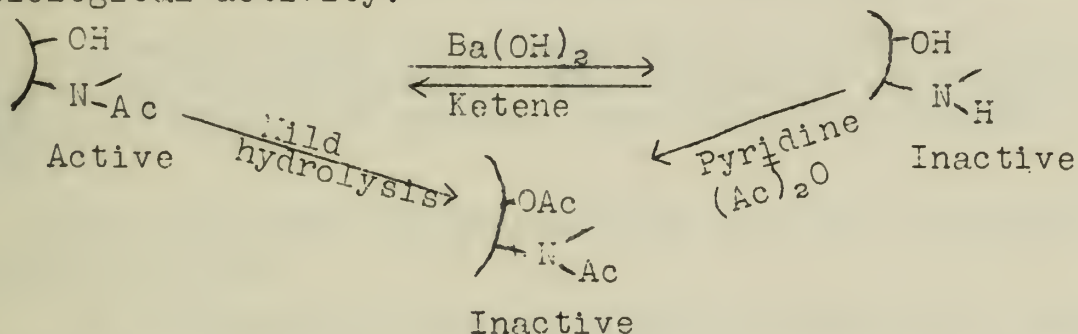
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physiological action. Normal degradation processes are of little value when applied to these substances. Reactions must be carried out on entire molecules, the result being interpreted in an altered physiological activity.

Degradation of insulin yields only the usual protein amino acids and a high disulfide content which is believed to be one of the points of activity. Spectral absorption has revealed that inactivation can occur without alteration of the spectrum but alteration is always accompanied by inactivation.

Reversible inactivation is accomplished by diazo methane and formaldehyde. Acetylation inactivates, but if only the O acetyls are removed activity again appears. Reduction and oxidation inactivate insulin irreversibly. Likewise enzymatic hydrolysis produces an irreversible inactivation.

Blood group substances, occurring primarily in red blood cells, are the substances responsible for the specific seriological nature of blood. Conflicting evidence exists as to the chemical nature of these substances, some claiming them to be protein in nature while Freudenberg characterizes them as nitrogen containing polysaccharides, having isolated galactose and an amino hexose from group A and B substances. Regardless of the nature, Freudenberg has demonstrated that an N acetyl group is necessary for physiological activity.



The success of present methods of attack in elucidating the structure of these physiologically active substances is dependent upon demonstrating that physiological action is the property of a specific constituent of the molecule. If one is forced to the conclusion that the physiological activity is a function of the entire molecule new methods of approach must be employed.

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Ann., 510, 240-248 (1934)
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Reported by D. J. Butterbaugh
F. J. Glavis
February 24, 1937.

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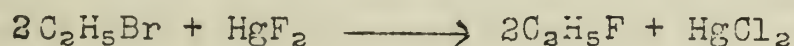
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ORGANIC FLUORINE COMPOUNDS

Bockemüller: Würzburg
 Midgley and Henne: Ohio State
 Swarts: Ghent

Organic fluorine compounds have been known for about fifty years, but they have become important only recently.

The preparation of alkyl fluorides is generally carried out by the reaction of metallic fluorides on alkyl chlorides, bromides or iodides. Hg_2F_2 , AgF , ThF , HgF_2 , SbF_3 , SbF_3Cl_2 have been used, the last three being the most important. The preparation of ethyl fluoride is an example:

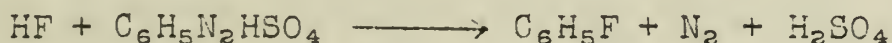


Fluorine and hydrofluoric acid are usually unsuitable for the preparation of alkyl fluorides; in most cases the reaction is violent and uncontrollable and no definite products can be isolated. This is to be expected, for the heat of reaction is greater than the energy required to rupture a carbon-carbon bond. However, cyclohexyl fluoride and hexadecyl fluoride have been prepared by the action of F_2 on the corresponding hydrocarbon.

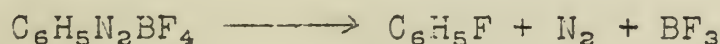
Fluorides cannot be prepared by the addition of HF or F_2 to olefins, tars being formed. The reaction of alcohols with anhydrous HF gives poor yields (less than 50 per cent) of the alkyl fluoride.

There are three general methods for the fluorination of the aromatic nucleus:

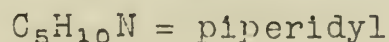
1. The decomposition of diazonium salts in concentrated aqueous HF solution:



2. The thermal decomposition of dry diazonium borofluorides:



3. The cleavage of diazoamino compounds with HF :



Aryl fluorides cannot be prepared by direct fluorination of the hydrocarbon.

Other types of fluoro compounds are known, such as fluoroacids and acid fluorides.

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-2-

Most important of the physical properties of organic fluorine compounds are their boiling points. All boil lower than the corresponding chlorides; in general the substitution of F for Cl lowers the boiling point about 45° . There is no corresponding regularity in the density or atomic refractivity, the latter even assuming apparent negative values at times. The steric effects of fluorine are slight, as might be expected from the small atomic radius.

The chemical properties of organic fluorides differ somewhat from those of other halides. The alkyl monofluorides are easily hydrolyzed and easily lose HF to form the olefin, but the presence of another negative group such as COOH, OH or halogen on the same carbon atom strengthens the C-F bond. If two fluorines are on the same carbon atom this effect is very marked; the difluoride is very inert and the reactivity of any other halogen on the same or adjacent carbon atoms is sharply decreased.

Reduction of vinyl or aryl fluorides usually results in the loss of HF. Fluorides undergo the Wurtz reaction, but more slowly than the corresponding chlorides. With zinc alkyl polyhalides containing fluorine lose the other halogens first to give the olefinic fluorides in good yields. Both alkyl and aryl fluorides form Grignard reagents, but the reaction is very slow.

The aryl fluorides have some technical importance as dye intermediates. Of the alkyl fluorides, CCl_2F_2 and some of the fluorochloroethanes have found wide use as refrigerants.

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Reported by C. L. Levesque
C. L. Fleming
March 3, 1937.

CONTRIBUTIONS OF DIPOLE MOMENTS TO ORGANIC PROBLEMS

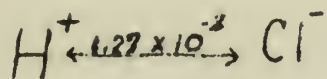
A dipole consists of two equal charges, relatively close together and opposite in sign. Its magnitude is measured by its moment, which is the product of either charge multiplied by the distance between them. The moment may be determined experimentally by the measurement of the dielectric constant and the density and the application of the Debye equation.

$$\frac{\epsilon-1}{\epsilon+2} \cdot \frac{M}{d} = a + \frac{b}{T}$$

where ϵ = dielectric constant T = absolute temperature
 M = molecular weight a = approximately the molar refraction
 d = density $b = 4\pi N M^2 / 9R$

The quantity on the left of the equation, which is called the molar polarization is plotted against the reciprocal of the temperature, the value for b is found and M is calculated.

A picture of the dipole may be obtained by regarding the hydrogen chloride molecule as made up of the positive charge of the proton and the negative charge of the chloride ion at a distance of 1.27×10^{-8} cms. The calculated moment would then be $1.27 \times 4.774 \times 10^{-18} = 6.06 \times 10^{-18}$ or 6.06 debyes. However, if one calculates the effect of the attraction of the outer chlorine electrons by the proton, a value of 1.09 is deduced. The observed value is 1.03.



Since benzene has a moment of zero and chlorobenzene has a moment of 1.52, the carbon-chlorine bond is assigned a value of 1.52. Now if additional chlorines are added to the ring, new dipoles are formed and the moment of the molecule is the resultant of the individual dipoles. The following table shows the agreement between observed and calculated values.

<u>Compound</u>	<u>Calculated</u>	<u>Observed</u>
<u>o</u> -C ₆ H ₄ Cl ₂	2.63	2.25
<u>m</u> -C ₆ H ₄ Cl ₂	1.52	1.43
<u>p</u> -C ₆ H ₄ Cl ₂	0	0

The fact that the observed ortho moments are less than the calculated is due to the lowering of each moment by shifts of the charge induced by each other.

Dipole moment is greatly influenced by the kinetic energy of the molecule. It has been found that when two dipoles can turn relative to one another, mutual repulsion tends to make the position of low resultant moment more probable. In the case of ethylene dibromide, the observed moment is much less than that which is calculated

A series of experiments have been made to determine the effect of temperature on the rate of crystallization of a magma. The results show that the rate of crystallization increases with increasing temperature, and that the rate of crystallization is also affected by the composition of the magma.

$$\frac{dX}{dt} = k(1-X)^n$$

where X = fraction crystallized, t = time, k = rate constant, n = order of reaction.

The results of the experiments show that the rate of crystallization is first order with respect to the fraction of magma remaining to be crystallized.

A series of experiments have been made to determine the effect of pressure on the rate of crystallization of a magma. The results show that the rate of crystallization increases with increasing pressure, and that the rate of crystallization is also affected by the composition of the magma.

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1. H. S. G. Mason, "The Crystallization of a Magma," *Philosophical Magazine*, vol. 1, p. 1, 1901.
2. H. S. G. Mason, "The Crystallization of a Magma," *Philosophical Magazine*, vol. 1, p. 1, 1901.
3. H. S. G. Mason, "The Crystallization of a Magma," *Philosophical Magazine*, vol. 1, p. 1, 1901.

Temperature	Rate of Crystallization	Order of Reaction
100°C	0.01	1.0
200°C	0.02	1.0
300°C	0.04	1.0

The results of the experiments show that the rate of crystallization is first order with respect to the fraction of magma remaining to be crystallized.

These results are in agreement with the theory of the earth's crust, which predicts that the rate of crystallization should increase with increasing temperature and pressure.

assuming free rotation between the carbon atoms. This is due to the fact that bromines are forced into the trans position which tends to cancel and lower the resultant moment. As the temperature is raised the kinetic energy tends to overcome the mutual repulsion and the value approaches that which is calculated for the free rotating model. As more methylene groups are put into the molecule, the mutual repulsion becomes less important and the observed value more nearly approaches the calculated.

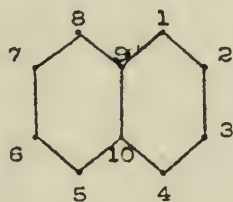
A great many para compounds yielded moments which can be explained by the fact that the valence angle of oxygen is 110° and, therefore, the moment does not operate in the plane of the nucleus.



Dipole moments have been instrumental in the solving of many structural problems.

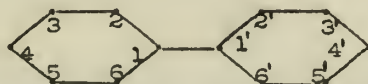
Benzene.--Since the moments which were calculated for m and p-dichlorobenzene agree so well with the observed, the benzene ring must be planar with the external valences also in the same plane.

Naphthalene:



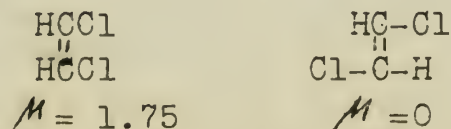
Since the 2,6 derivatives have no moment and the 1,8 derivatives have a moment which is twice that of the 1-mono derivative, both rings of the naphthalene nucleus are in the same plane.

Biphenyls:



The fact that 4,4'-substituted biphenyls have no dipole moment shows that the biphenyl molecule must be an extended one. The measurement of the 2,2'-substituted derivatives shows that all positions of rotation are not equally probable.

Cis-trans isomers:



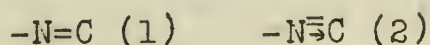
These may be distinguished by the fact that the cis form always has the larger moment.



Nitro groups.--Since *p*-dinitrobenzene does not have a dipole moment, the dipole due to the nitro group must act in a line with the nitrogen valence joining the group to the ring. This, apparently, means that a valency bond is continually oscillating between the two oxygen atoms.

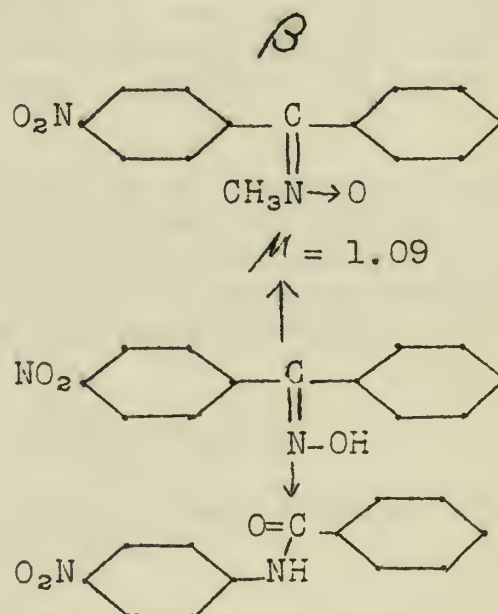
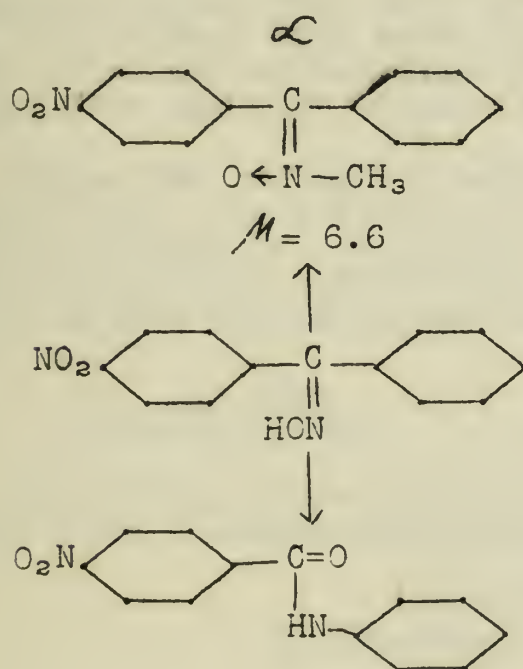


Isocyanide groups.--There are two possible formulas for the isocyanide group.



In the case of the second formula the dipole acts in a line with the remaining valence bond of nitrogen. Since the moment of *p*-diisocyanobenzene is found to be zero the second formula is considered correct.

Beckmann rearrangement.--The following diagram shows that the Beckmann change is a trans and not a cis migration.



Since the α compound has a large dipole moment the NO_2 and NO , both powerfully polar groups, are assumed to be on the same side and adding. In the β form the groups neutralize and give a smaller resultant moment.

The major contribution of dipole moments has been its aid in determining the shapes of molecules and of various groups on the molecule. The work in the last ten years has improved its manipulation to such an extent that it should become an important tool in structure determination.

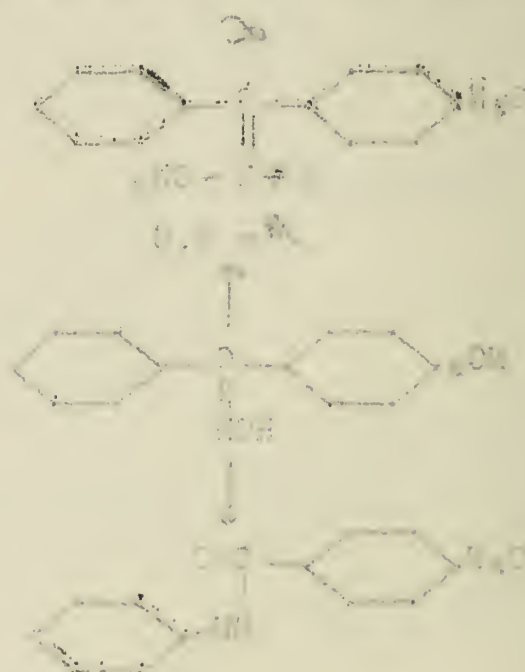
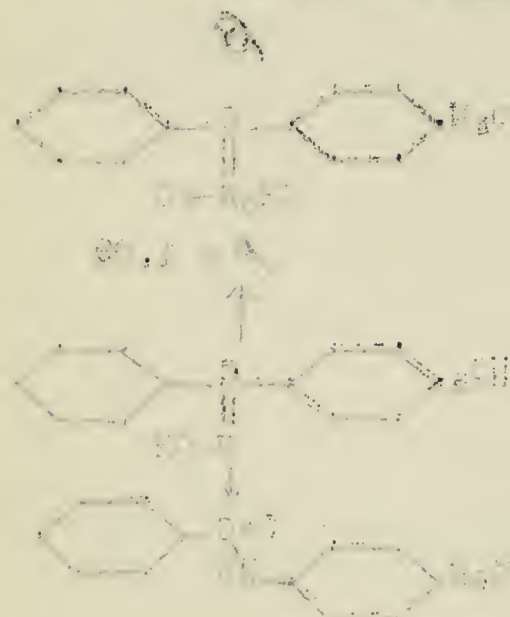
Bibliography: Smyth (Princeton, J. Org. Chem, 1, 17 (1936)
Glasstone (Sheffield), Recent Advances in Physical Chemistry
Sidgewick (Oxford), Chem. Reviews, 19, 183 (1936)

Reported by C. E. Denoon, Jr.
March 10, 1937.

between the two groups of people, and the fact that the two groups of people are not the same.



(3) 574. (4) 575.



AUXIN "a", "b"; AUXIN GLUTARIC ACID; HETEROAUXIN

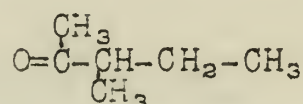
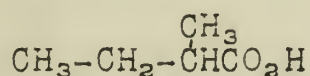
Kögl and associates (Utrecht), Z. physiol. Chem., 227, 51 (1934)
 " " " " " " " , 235, 181 (1935)
 " " " " " " " , 235, 201 (1935)

It is a fact of plant physiology that the growth-regulating, root-forming chemical substances are formed in the leaves of plants and transmitted backwards. Kögl and his associates isolated from the tips and leaves of plants two crystalline compounds which they called auxin "a" and auxin "b".

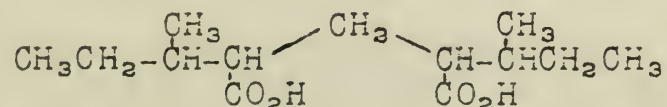
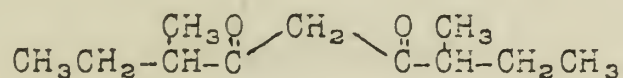
Because of the relatively small amount of auxins in the plants themselves Kögl was unable to isolate a very large quantity of them. Accordingly there are a few places in the proof of the structure of these hormones which have not been thoroughly confirmed due to a lack of starting material.

From preliminary experiments it was known that the auxins are monobasic acids; they have one double bond, a carbocyclic ring, form δ lactones; that auxin "a" has three hydroxyl groups and that auxin "b" loses carbon dioxide on heating. Oxidation of both compounds gave the same dibasic acid.

These two carboxylic acids were shown to be separated by 5 carbon atoms. As a result of several procedures the dibasic acid was transformed into a di-glycol which gave a 1,3-diketone with lead tetraacetate. Hydrolysis of this diketone gave an optically active methyl pentanone and dextro α methyl butyric acid



By putting these pieces together the original dibasic acid was found to be a substituted glutaric acid, thus



Because of the large number of isomers possible this was simply called auxin glutaric acid.

This acid was synthesized. Experimental results limited the theoretically 10 possible stereoisomers to 3. With dextro α methyl pentanoic acid as the starting material the three expected stereoisomeric acids were made and separated. One of these was identical with the auxin glutaric acid of degradation.

It is a fact of some importance that the land in the State of New York is not only abundant but also of high quality. The land is not only abundant but also of high quality. The land is not only abundant but also of high quality.

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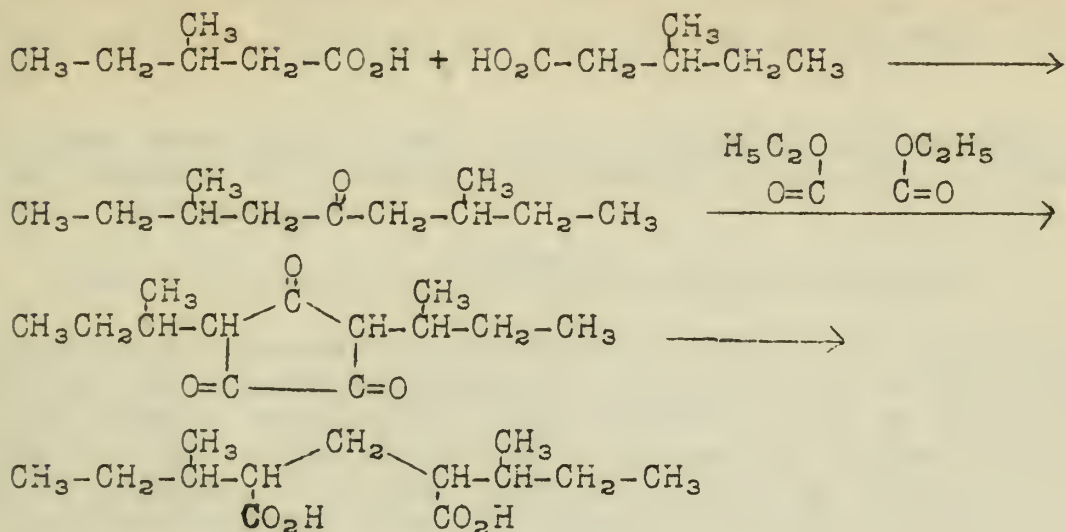
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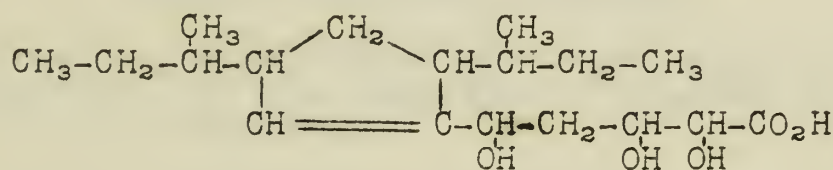
It is a fact of some importance that the land in the State of New York is not only abundant but also of high quality. The land is not only abundant but also of high quality. The land is not only abundant but also of high quality.

In brief the synthesis of this can be represented thus:

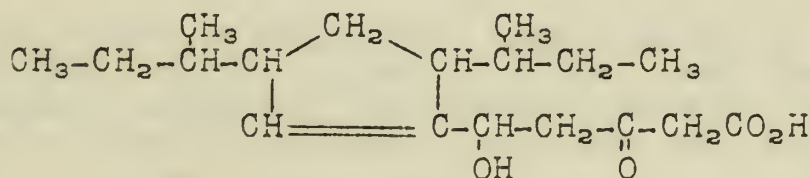


The side chain of auxin "b" has not been investigated as critically as could be expected. That of auxin "a" has been confirmed by degrading the reduced auxin "a".

The following formulas are proposed for the auxins:

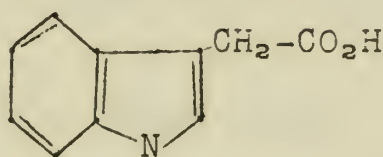


Auxin "a"



Auxin "b"

β indolyl acetic acid called heteroauxin and a number of its derivatives together with α naphthyl acetic acid and phenyl acetic acid have been shown to have plant hormone activity



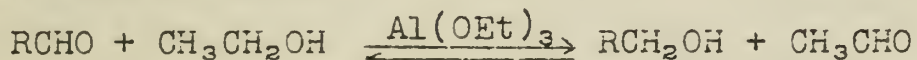
Heteroauxin

2000

I. Alcoholates

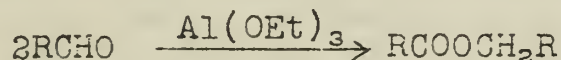
Reductions catalyzed by metal alcoholates have been studied simultaneously by Ponndorf and Verley and by Meerwein and co-workers.

It has been shown that either aldehydes or ketones may be reduced by primary or secondary alcohols using metal alcoholates as catalyst. For example:



The reaction is reversible but may be driven to completion by distilling the volatile aldehyde. Ketones and some aldehydes are more efficiently reduced by isopropylates than by ethylates. This is probably due to the fact that the acetone formed by isopropylate reduction is less easily reduced by the reverse reaction than is acetaldehyde. The benzylates are also vigorous reducing catalysts.

This reaction differs from the Titschenko condensation of aldehydes to esters in that the latter does not use an alcoholic solvent and is carried out at higher temperature.

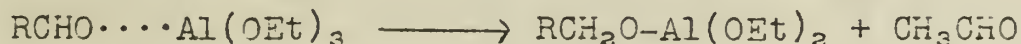


A great variety of metal alcoholates have been found to promote the reduction, but the compounds of aluminum and magnesium appear to be the most effective.

The outstanding advantage of this method is that the reagent specifically reduces the carbonyl group and does not attack other points of unsaturation in the molecule.

Examples of compounds which have been reduced by this method are: crotonaldehyde, citral, nitro-, chloro-, and bromo-substituted cinnamic aldehydes, halogenated acetone, menthone and carvone. Amino or phenolic groups hinder the reducing action.

Several reaction mechanisms have been proposed. That which seems to be supported by the most evidence (Meerwein, 1936) is represented by the equations:

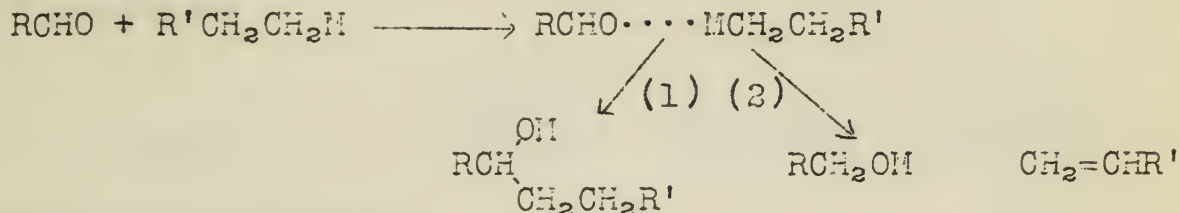
II. Metal Alkyls

Many investigators have reported instances in which Grignard reagents have shown a reducing action on carbonyl compounds. Their attempts to find definite correlation between the amount of reduction and the complexity of the carbonyl compound and Grignard reagent were unsuccessful. Isolated instances have been reported of similar reductions involving metal alkyls and carbonyl compounds.

-2-

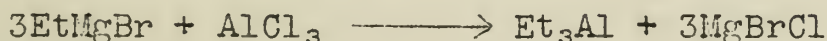
For instance zinc ethyl reduces chloral to give trichloroethyl alcohol, evolving ethylene in the process.

The most probable mechanism for the reaction is that suggested by Meisenheimer:

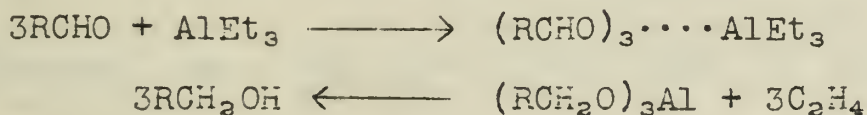


in which the hypothetical addition product may rearrange according to (1) to give a normal reaction or eliminate an olefin according to (2) to give reduction. Confirmation of this mechanism is found in the fact that the addition compounds have been isolated in the cases of acetomesitylene and Michler's ketone with some Grignard reagents. On the basis of this conception it would be expected that the nature of the metal alkyl would determine which course the reaction would take. From analogy to metal alcoholates, Meerwein assumed that the amount of reduction would decrease with increased polarity of the metals and carried out a series of reactions to determine whether or not such a relationship existed.

Aluminum and boron triethyls were used extensively because they caused appreciable reduction. Aluminum triethyl was prepared according to the following scheme:

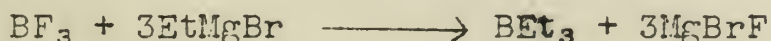


The reducing action of aluminum triethyl evidently followed the scheme:

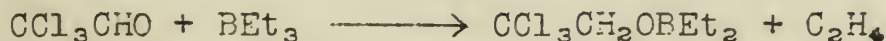


because colored solutions were obtained on mixing the carbonyl compound and aluminum triethyl and these colors disappeared on evolution of ethylene.

Boron triethyl was prepared according to the scheme:



Boron triethyl behaved analogously to aluminum triethyl, but only one ethyl group was affected.



The diethyl boric acid esters which were formed were easily hydrolyzed with water to give the corresponding acid and alcohol. In this case also, addition products were indicated by the colors which developed on mixing the reactants.

Such substances as bromal, chloral, trichloroacetone, mono-chloroacetone, benzil, benzaldehyde, etc., were treated with these reagents to give high yields of the corresponding alcohols. The following table shows the relationship between the reducing action of various metal alkyls and the electropositiveness of the metals involved:

Metal Alkyl	with	Per cent Normal Reaction	Per cent Reduction	Ethylene Evolved
BEt ₃	p-chlorobenzaldehyde	0	90	84
ZnEt ₂	"	38	45	?
AlEt ₃	"	51	25	21
EtMgBr	"	90	0	0
SnEt ₄	bromal, chloral	0	0	0

In the case of tin tetraethyl evidently the metal is too strongly attached to the alkyl groups for either reaction to take place.

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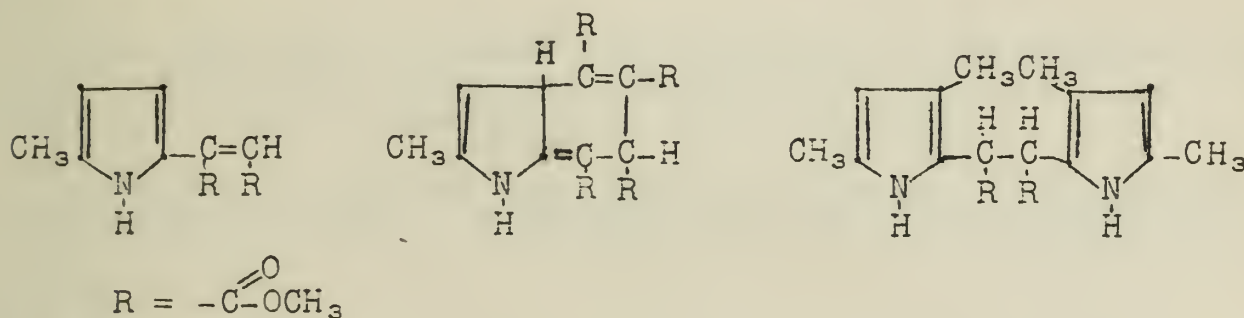
- Meerwein and coworkers (Harburg), J. prakt. Chem., 147, 203, 226 (1936)
 Ponndorf, Zeitschr. angew. Chem., 39, 138 (1926)
 Meisenheimer, Ann., 442, 189 (1925); 446, 76 (1926)
 Blatt and Stone, J. Am. Chem. Soc., 54, 1495 (1932)

Reported by Wayne Cole
 John Anderson
 March 17, 1937.

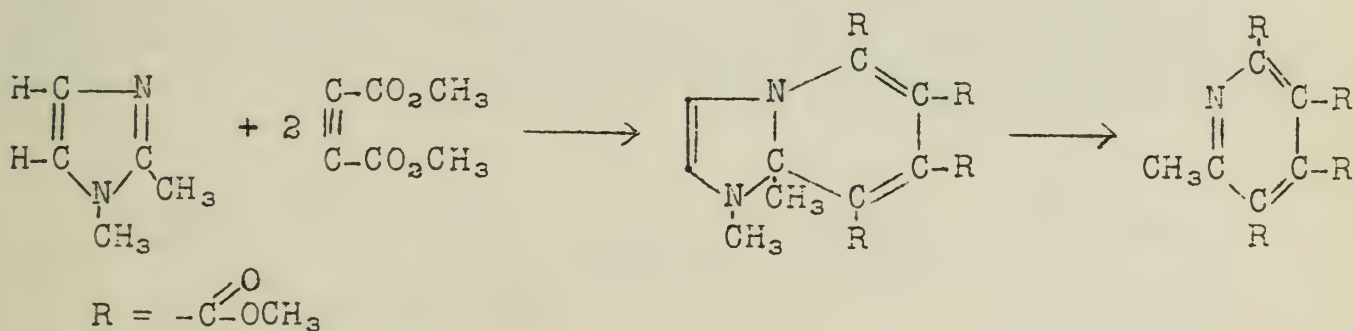
WITH ACETYLENE DICARBOXYLIC ESTER

O. Diels and K. Alder - University of Kiel

For the last several years Diels and Alder have been making a comprehensive study of the "diene synthesis," which involves the 1-4 addition of an "activated" double bond to a conjugated double bond system. Having found that furan reacts normally with maleic anhydride or acetylene dicarboxylic ester, they were surprised to note that pyrrole and homologs react abnormally, giving one of the following products, according to the proportion of reactants used:

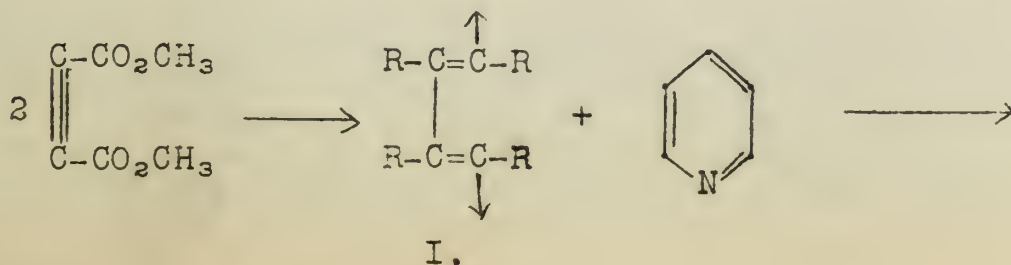


Furthermore, from 1,2-dimethyl imidazole and acetylene dicarboxylic ester they isolated a bicyclic addition product, from which the imidazole residue could be cleaved, leaving a substituted pyridine:



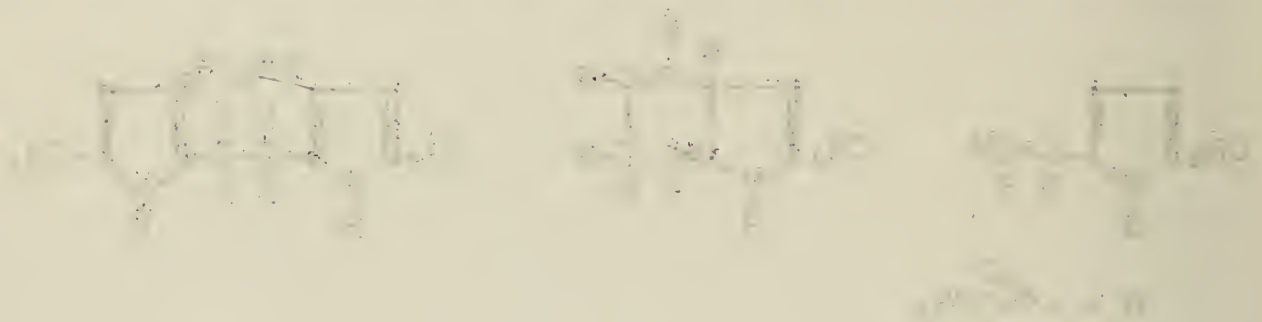
These results led them to try the action of acetylene dicarboxylic ester on pyridine and its homologs.

The products of this reaction depend on the solvent used in glacial acetic acid, the sole product is the hexamethyl ester of mellitic acid. If, on the other hand, the reaction is carried out in ether, three addition products appear, all resulting from the combination of one mole of base with two of ester. Diels and Alder represent the reaction thus:



THE LAND OFFICE, ALBANY, N. Y., JANUARY 1, 1882.

For the year 1881, the land office has been engaged in a comprehensive survey of the lands of the State, and has been successful in obtaining a large amount of valuable information. The survey has been conducted in accordance with the plan adopted at the last session of the Legislature, and has been completed in a large measure. The results of the survey are now being prepared for publication, and will be ready for the press in a few weeks.

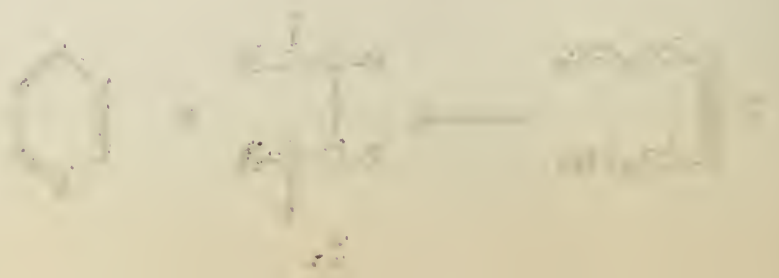


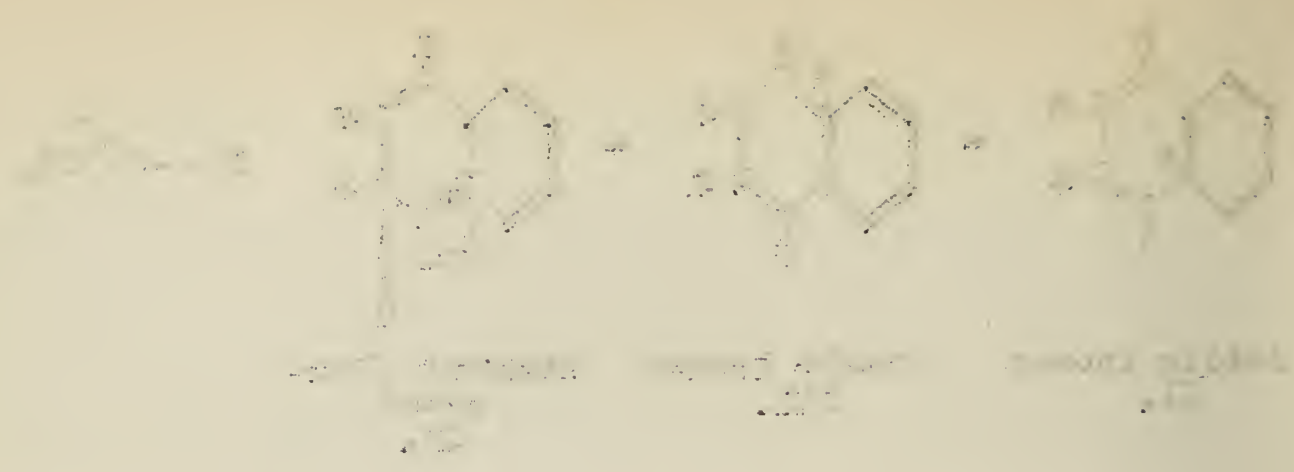
The above reaction is a typical example of the action of a strong base on a substituted benzene ring. The base abstracts a proton from the nitrogen atom, leading to the formation of a carbanion. This carbanion then reacts with the reagent to form the final product.



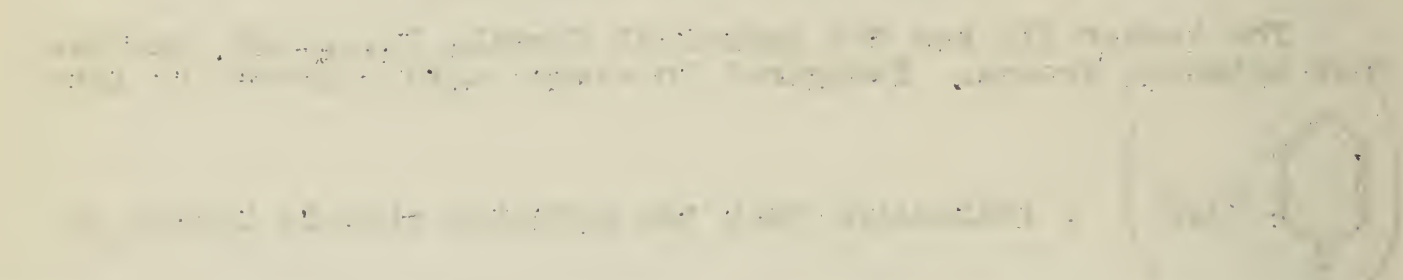
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The first two structures are isomers of the same molecular formula, $C_{10}H_{10}O_2$. The third structure is a dimer of the first two.

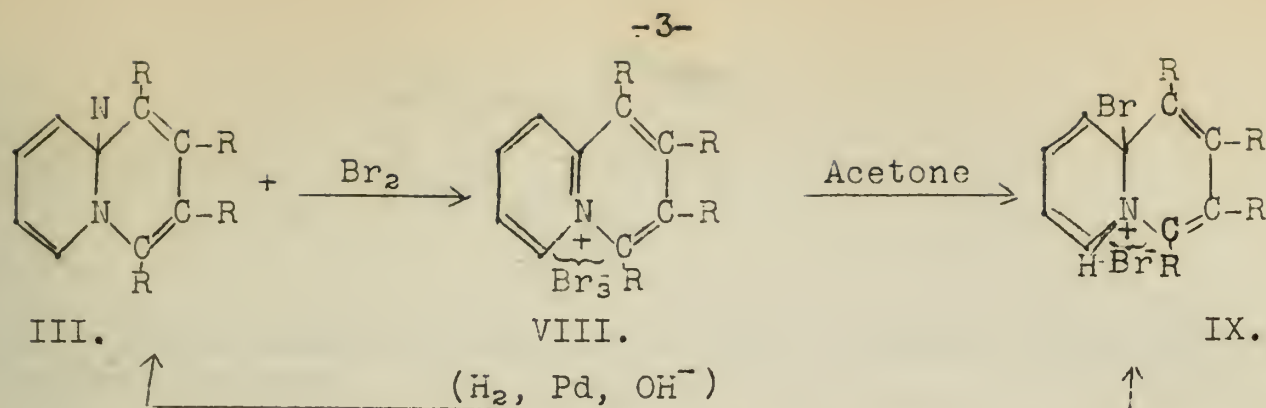


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References

1. J. H. R. Taylor, *Journal of Organic Chemistry*, **1958**, *23*, 1234.
 2. J. H. R. Taylor, *Journal of Organic Chemistry*, **1959**, *24*, 1234.
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 8. J. H. R. Taylor, *Journal of Organic Chemistry*, **1965**, *30*, 1234.
 9. J. H. R. Taylor, *Journal of Organic Chemistry*, **1966**, *31*, 1234.
 10. J. H. R. Taylor, *Journal of Organic Chemistry*, **1967**, *32*, 1234.

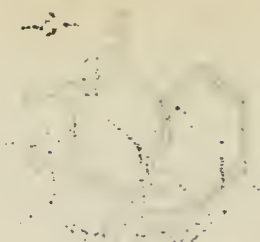


The non-ionic bromine of IX is very labile; in methanol in the cold it is replaced by a methoxyl. Treatment of IX with pyridine gives IV, the "Kashimoto compound," which was also obtained as one product of the original reaction.

The "Kashimoto Compound," IV, has the empirical formula $\text{C}_{16}\text{H}_{13}\text{O}_8\text{N}$, and contains but three methoxyl groups, and no free carboxyl, as evidenced by its inactivity to diazomethane. It may also be obtained directly from III by dehydrogenation with PbO_2 or azodicarboxylic ester. If it be treated with NaOMe in MeOH , and then HClO_4 , there is obtained the same perchlorate as that obtained from treatment of the perbromide VIII with HClO_4 . On the basis of these reactions, Diels and Alder propose for it the inner salt formula IV shown above.

The "labile isomer," II, has the same empirical formula as the "stable isomer," III. From the facts that: 1) it may, under proper conditions, be the sole product of the reaction, and 2) it is readily converted into III on heating; it was considered a precursor of III. It does not form salts with acids. Treatment with strong alkali gives as products pyridine, aconitic acid, and oxalic acid; no α -picolinic acid was isolated (this being the product of alkaline degradation of III). This shows that in the labile isomer there is no substituent on the α -carbon; that II does not form acid salts is indicative of a pentavalent nitrogen. The isolation of aconitic acid indicates that the two acetylene dicarboxylic ester molecules are linked together, and not separately to the nitrogen. These considerations led Diels and Alder to propose the "penta-alkyl ammonium" formula II shown above. II, then, is a totally organic substituted ammonium compound with one ionically bound substituent, similar to compounds made by Schlenk and Holz by the action of metal alkyls on ammonium salts; for example, triphenylmethyl-tetramethyl-ammonium.

If the reaction between pyridine and acetylene dicarboxylic ester is run in cold methanol, instead of ether, a different product is isolated, having the formula $\text{C}_{16}\text{H}_{17}\text{O}_7\text{N}$, and four methoxyls. Similar to III, on treatment with perhydrol, it is converted to α -picolinic acid-N-oxide. Contrary to III, this compound X is resistant to chromic acid oxidation and to the dehydrogenating action of azodicarboxylic ester. Diels and Alder interpret this as caused by lack of the hydrogen attached to the bridge carbon in III. From this, and the two following reactions, they proposed for X the formula:



176

177

178

179

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The following table shows the results of the experiments conducted on the effect of the various factors on the rate of reaction. The first column gives the number of the experiment, the second column gives the concentration of the reactants, the third column gives the temperature, and the fourth column gives the rate of reaction.

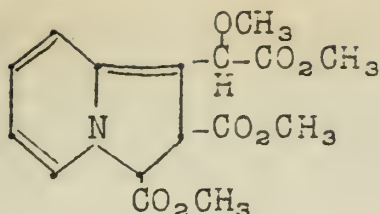
The results of the experiments show that the rate of reaction increases with increasing concentration of the reactants and with increasing temperature. The rate of reaction also increases with increasing surface area of the reactants. The rate of reaction is also affected by the presence of a catalyst.

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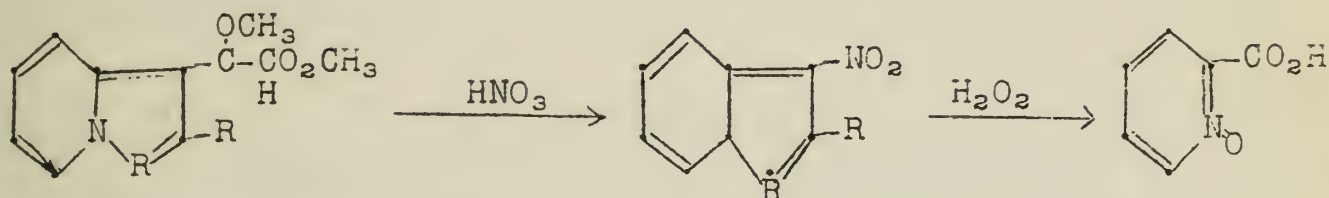
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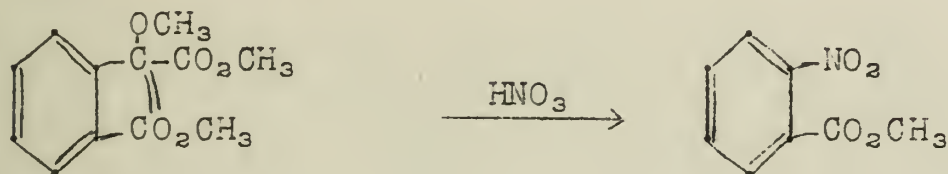
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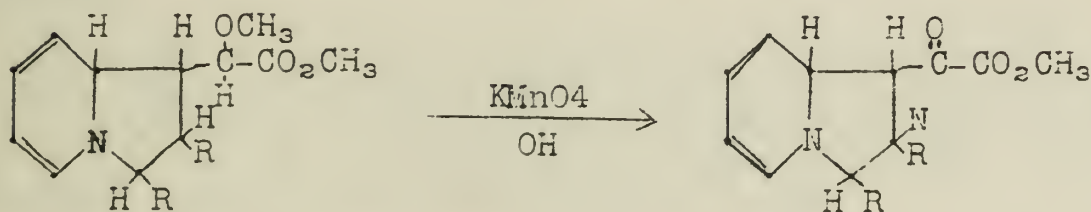
1. Nitric acid converts X to a nitro compound containing two methoxyl groups.



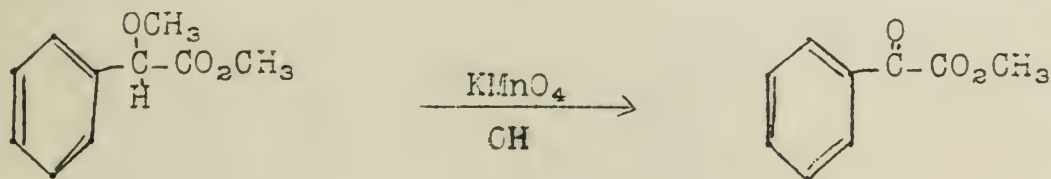
The second reaction shows that the pyridine ring is intact and that the nitro group was not in it. A similar reaction was observed by R. Meyer:



2. Alkaline permanganate on tetrahydro X gives an α -keto ester:



This is analogous to a reaction carried out by R. Meyer:



Quinoline and acetylene dicarboxylic ester in ether give two products analogous to the stable and labile products of the pyridine series.

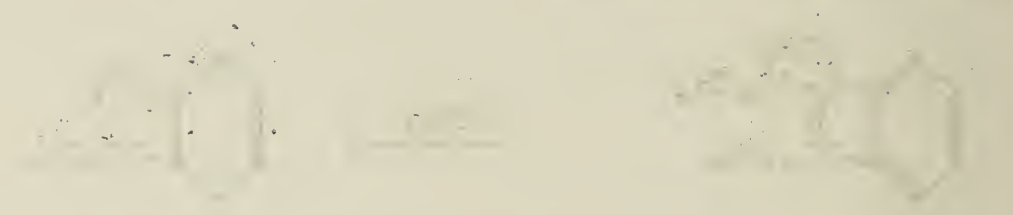
α -Picoline reacts vigorously with acetylene dicarboxylic ester, but no definite products could be isolated. That this vigorous reaction was ascribable to the reactivity of the methyl hydrogens was indicated by the fact that stilbazole (benzal- α -picoline) undergoes the reaction similar to pyridine.



Chemical structure of a substituted benzene ring with a side chain.



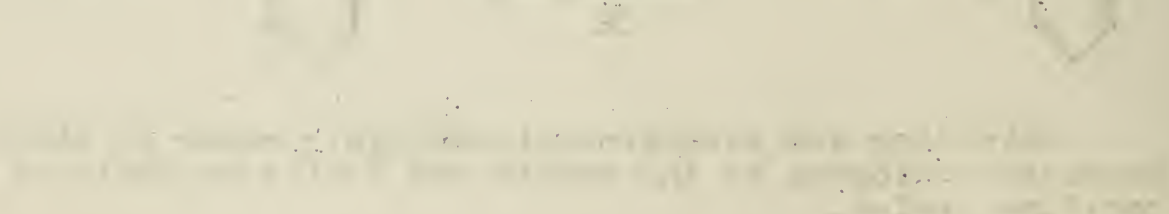
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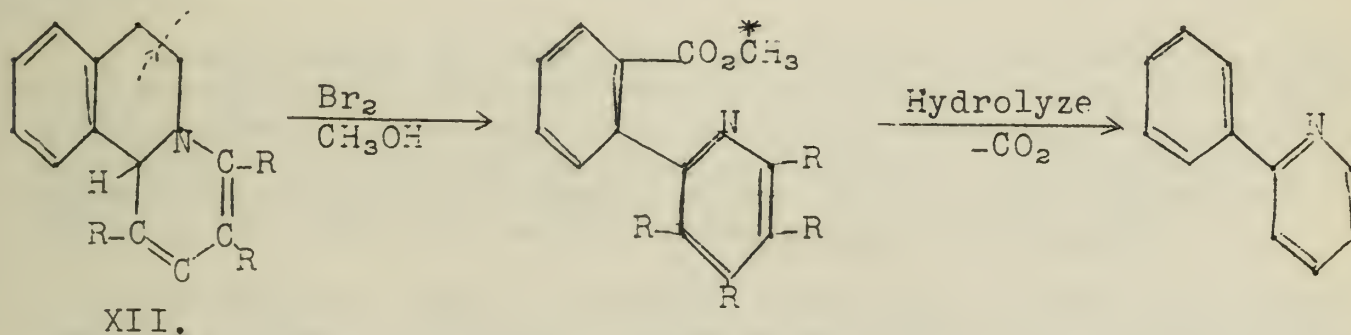
Chemical structure of a substituted benzene ring with a side chain.



Chemical structure of a substituted benzene ring with a side chain.

Quinaldine reacts to give one product showing the general characteristics (absorption spectrum, solubility, etc.) of a labile isomer, and two other products, whose formulas are uncertain. The labile isomer of quinaldine is, in contrast to that of pyridine, thermostable, possibly because of the absence of the α hydrogen.

The reaction with isoquinoline is more complex. The principal product is a labile isomer, XI, characterized by absorption spectrum and solubility. On heat treatment it gives two products, the principal one, XII, being a compound giving reactions similar to those of the pyridine stable isomer. Its structure was confirmed by the following reaction:



If run in Br_2 and EtOH , the OCH_3^* is OC_2H_5 . The structure of the second product from stabilization of XI has not been determined. In addition to XI, a second labile isomer results from the original reaction; this has a tendency to revert to its components; it can be converted by heat, with very low yield, into XII, although Diels considers this a complete decomposition, followed by formation of XI and its stabilization. The structure of this labile isomer is uncertain.

Although no synthetic applications of this reaction have as yet been made, it offers a short cut method to fused ring systems with a nitrogen as a common atom between two rings. No mention is made of the use of any unsaturated compound besides acetylene dicarboxylic ester on these nitrogenous bases.

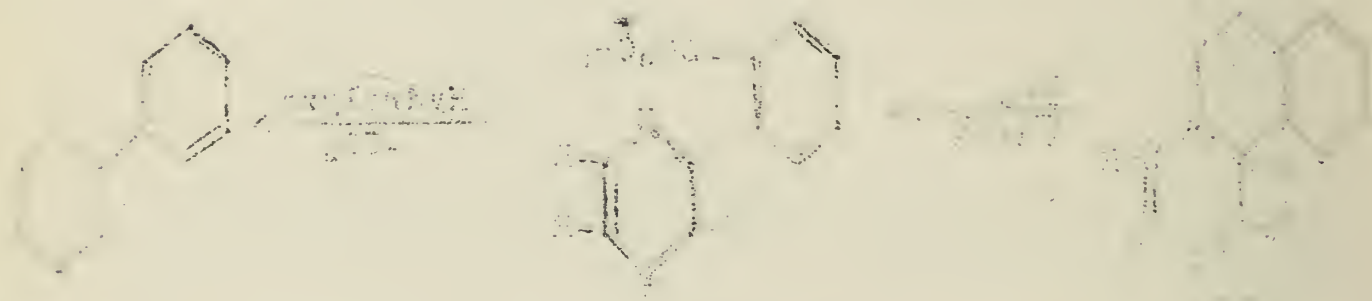
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 Diels and Alder, Ann., 505, 103 (1933)
 Diels and Alder, Ann., 510, 87 (1934)
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Reported by E. C. Kirkpatrick
 R. M. Joyce
 March 24, 1937.

The results of the study of the effect of the concentration of the solution of the substance on the rate of its reaction with the reagent are given in Table I. It is seen from the data that the rate of the reaction increases with an increase in the concentration of the solution of the substance. This is due to the fact that the rate of the reaction is proportional to the concentration of the substance.

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THE EFFECT OF WEIGHT

It is generally thought that three factors affect the dissociation of hexaarylethanes into the corresponding free radicals, and these are namely:

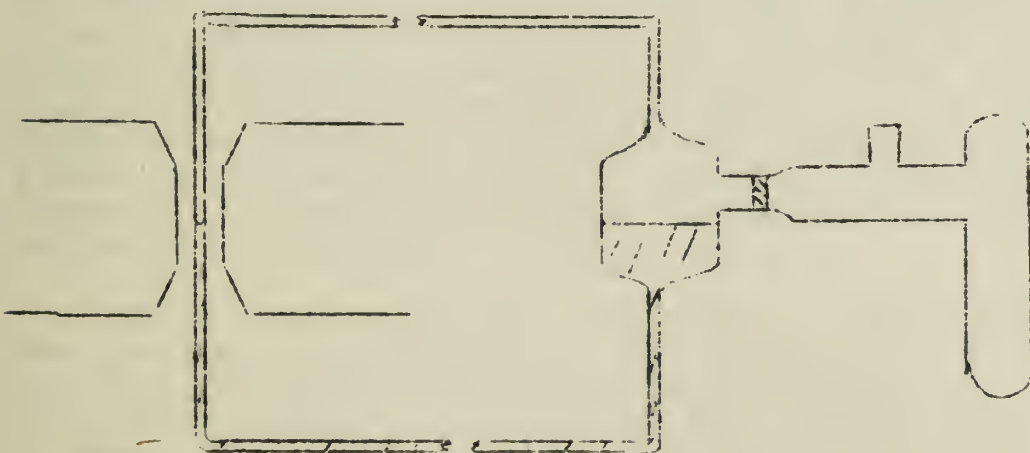
1. the unsaturation in the aryl groups
2. the weight of the aryl groups
3. steric hindrance between the aryl groups.

A large number and variety of hexaarylethanes have been prepared by various investigators to test the influence of these factors.

In an attempt to determine the effect of the weight of the aryl groups on the dissociation of the ethane, a series of hexa-p-alkyl-phenylethanes with the alkyl group varying from ethyl to sec-butyl were prepared in this laboratory.¹ In this series the unsaturation remains constant, steric effects are reduced to minimum, and only the weight of the groups is changed.

The depth of color of benzene solutions of the same concentration of these compounds increased with the size of the alkyl group, and hence it was postulated that as the weight of the aryl groups increased the dissociation of a hexaarylethane increased.

The degrees of dissociation have since been measured by a modification of the method developed by Eugen Müller.² The magnetic susceptibilities of 0.1 M solutions of the ethanes were measured by the so-called Quincke hydrostatic method. The apparatus used may be schematically diagrammed as follows:



The change in the height of the meniscus in the field on the application of a known magnetic field is measured by means of a cathetometer and the magnetic susceptibility of the solution may be calculated from the equation

$$\chi = \frac{2h}{gH^2} + \frac{d_0}{d} \chi_0$$

where X is mass susceptibility, h is the change in meniscus height on application of a field of strength H , g is the acceleration due to gravity, d is the density of the solution, and d_0 and X_0 are the corresponding quantities for the gas above the solution.

From the magnetic susceptibility and concentration of the solution, the degree of dissociation, α , may be calculated.

The results are summarized as follows:

hexaphenylethane	2.1 \pm .5 per cent
hexa- <u>p</u> -ethylphenylethane	3.4 \pm .3 per cent
hexa- <u>p-n</u> -propylphenylethane	4.2 \pm .6 per cent
hexa- <u>p</u> -isopropylphenylethane	4.2 \pm .5 per cent
hexa- <u>p-n</u> -butylphenylethane	5.0 \pm .2 per cent
hexa- <u>p</u> -isobutylphenylethane	6.8 \pm .5 per cent
hexa- <u>p-sec</u> -butylphenylethane	6.0 \pm .6 per cent
hexa- <u>p</u> -cyclohexylphenylethane	

References:

1. Copenhaver, Roy, Marvel, J. Am. Chem. Soc., 57, 1311 (1935)
2. Müller, Müller, Rodloff, Ann., 521, 89 (1935).

FREE ALKYL RADICALS

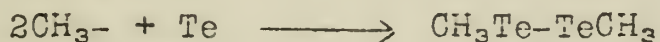
The term radical dates back to the time of Lavoisier. In 1832, Liebig and Wöhler¹ showed that when benzaldehyde was converted to a series of related compounds that the benzoyl radical was still present. A short time later Laurent² claimed that he had obtained the free benzoyl radical; actually he had obtained benzil. Franklin³ in 1849 heated ethyl iodide to 150° with zinc and obtained and described what he thought to be the free ethyl radical. Kolbe⁴ electrolyzed acetic acid and obtained a gas which he regarded as the methyl radical. Shortly after these articles, Gerhardt, Laurent, and Hofmann expressed the idea that these radicals in reality were "twin radicals."

From 1860 to 1900 the postulate of the quadrivalent carbon was developed and accepted. The application of this idea discouraged any further interest in free radicals. It was not until 1900 when Gomberg⁵ isolated the free triphenylmethyl radical that interest was again revived. The free radicals have been limited to compounds containing at least two aryl groups. Hexa-terbutylethynylethane showed only a weakened carbon to carbon bond.⁶

Except for a few isolated cases, the methods of classical organic chemistry have been fruitless in the preparation of aliphatic free radicals. In 1929, Paneth and coworkers⁷ were able to obtain the free methyl radical from the reaction:



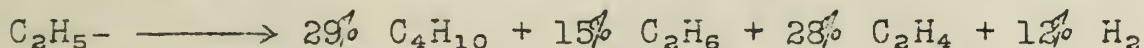
A one per cent solution of tetramethyl lead in acetone, heptane or hydrogen is passed down a quartz tube at 1-2 mm. pressure. It is heated to 500-600° by the means of an electrical furnace and immediately reacted with a metallic mirror which is cooled by water. The free radicals react with the metallic mirror in the following manner:



The dimethyl ditelluride was collected in a liquid air trap, its melting point determined and the compound analyzed. Various other metals have been used, antimony, arsenic, tellurium, lead, bismuth, mercury, tin and cadmium, but tellurium and recently lead have been found to work the best.

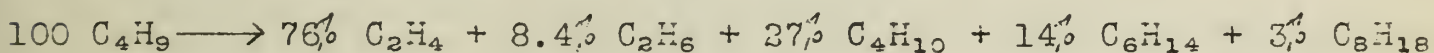
Paneth and Hafeditz⁸ showed that the half-life period of these radicals could be calculated according to the unimolecular reaction formula. If the free methyl radicals were allowed to react with themselves in a stream of hydrogen the only possible products are methane, ethane, ethylene and hydrogen.

Careful investigations of lead tetraethyl showed the formation of butane as well as ethane, ethylene and hydrogen.

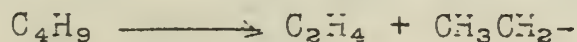


Reaction with metallic mirrors gives the corresponding ethyl derivatives.

Continuation of the study of the higher lead alkyls was prevented by the difficulty involved in the preparation and pyrolysis of the compounds. However, Frey and Hepp⁹ have shown that the mercury alkyls are capable of pyrolysis to form free radicals. Di-n-butyl mercury and di-sec-butyl mercury vapors were passed through a pyrex tube at 3 mm. and 490°. The special columns of Frey and Hepp enabled them to separate the many products.

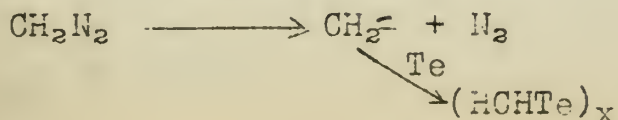


Most of the primary decomposition goes according to the equation:



With sec-butyl radicals the yield of 3,4-dimethylhexane is 23 per cent hence the radical is more stable than the normal radical.

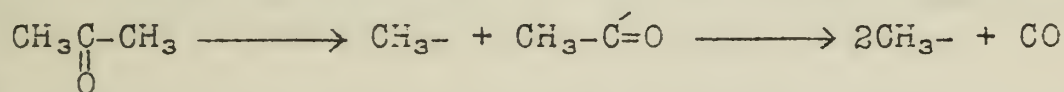
Rice and coworkers have been instrumental in the development of many of the free radical mechanisms. They suggested that the primary dissociation of methane could not give the methylene radical and hydrogen. This they showed by the pyrolysis of methane¹⁰ to give dimethyl ditelluride and no telluroformaldehyde. However, they were able to obtain the methylene radical¹¹ by the pyrolysis of diazomethane.



It does not, however, react with benzoic acid.¹²



Recent work by Pearson and coworkers has shown that the primary photochemical processes in the decomposition of ketones¹³ behaves similarly to the metal alkyls. By passing vapors of acetone through a quartz tube at 2 mm. pressure and activating the molecule by ultra-violet light it was possible to detect, by use of metallic lead, free methyl radicals 35 cm. from the irradiated zone.



The lead dimethyl was reacted with mercuric bromide to obtain the methyl mercuric bromide and its melting point determined. They have determined the half-life periods of methyl, ethyl, propyl and isopropyl radicals and have found fair agreement with the values of Paneth.

methyl	5.3 x 10 ⁻³	sec.
ethyl	3.3 x "	"
propyl	4.0 x "	"
isopropyl	4.4 x "	"

"The radical theory is capable of interesting application in various branches of chemistry. Undoubtedly important is its extension to the field of reaction kinetics." F. A. Paneth.

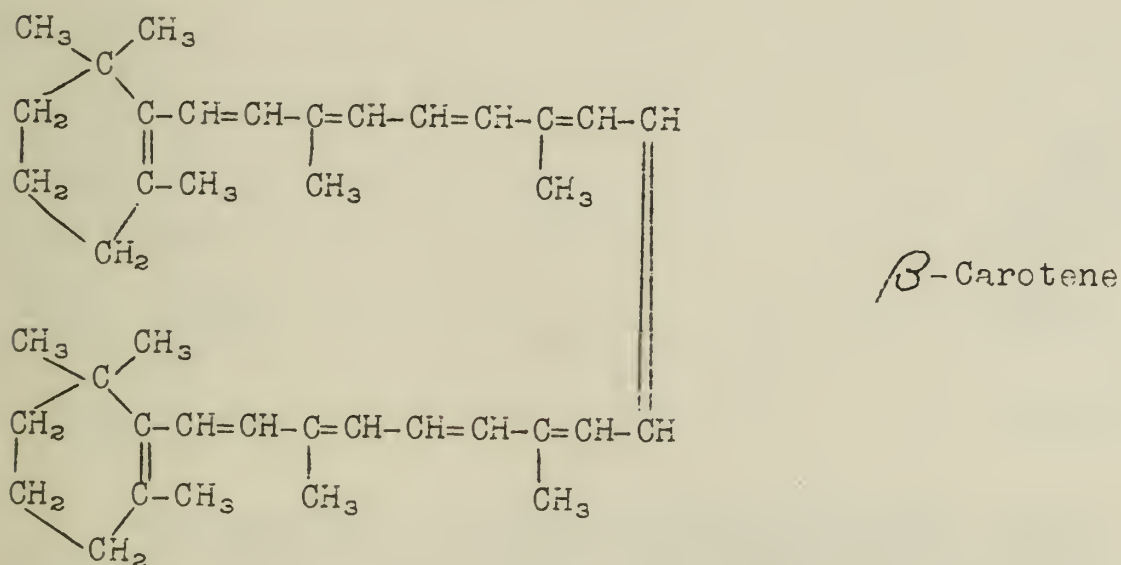
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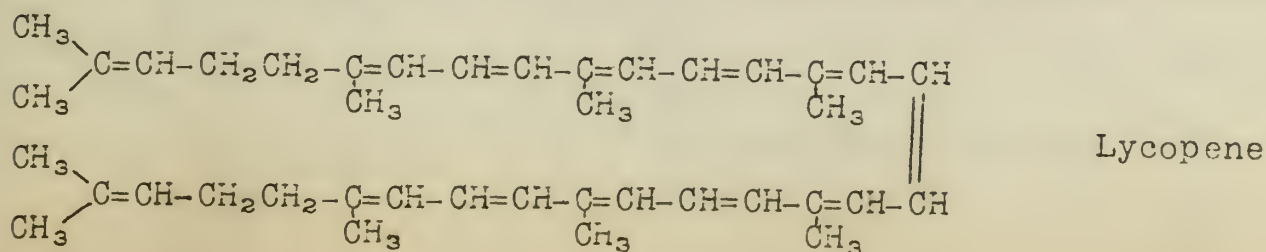
Reported by M. F. Roy
L. R. Drake
March 31, 1937.

Six carotenoid pigments were known when Palmer published his book on the subject in 1922. Early workers were R. Wallstatter and his students who, before the late war, purified a series of carotenoids and determined their formulae. The impetus to further investigation came from Karrer's and Kuhn's work on bixin and crocetin, from which it was established that the conjugated double bond can act as a chromophore if present in a sufficient number. Thirty naturally-occurring carotenoid pigments are now known, fifteen of which have been isolated in the past three years. The microanalytical methods developed by Pregl and the chromatographic separation technic became powerful tools in the characterization and elucidation of the structures of these compounds.

The structures of the isomeric carotenes, when once established, enabled investigators to relate most of the remaining carotenoids to these. β -Carotene was found on catalytic hydrogenation to take up 11 moles of hydrogen, 8 of which remove all color. The product is a paraffin, $C_{40}H_{78}$. From this it was concluded that the compound contained two rings and that three double bonds do not contribute to the color. Degradation by oxidation was successful only after much experimentation. Products identified were dimethyl malonic, α,α -dimethyl succinic, α,β -dimethyl glutaric, and geronic acids, which are all known likewise to be oxidation products of β -ionone. The odor of the latter was often noticed. The postulated structure was established later from further evidence.



More clear-cut work on the closely related lycopene justified the symmetrical formula assigned to the above. Lycopene takes up 13 moles of hydrogen to give the paraffin $C_{40}H_{78}$ and on ozonization yields an amount of acetone in agreement with the formula



The first of these is the question of the origin of the human race. It is generally admitted that the human race is descended from a common ancestor, but the question of the exact nature of this ancestor is still a matter of debate. Some authorities believe that the human race is descended from a single pair of individuals, while others believe that it is descended from a larger number of individuals. The question of the origin of the human race is one of the most important questions in anthropology, and it is one which has attracted the attention of many of the most distinguished scientists of the present day.

The second of the questions mentioned above is the question of the development of the human race. It is generally admitted that the human race has developed from a lower state to a higher state, but the question of the exact nature of this development is still a matter of debate. Some authorities believe that the human race has developed from a lower state to a higher state, while others believe that it has developed from a higher state to a lower state. The question of the development of the human race is one of the most important questions in anthropology, and it is one which has attracted the attention of many of the most distinguished scientists of the present day.

The third of the questions mentioned above is the question of the classification of the human race. It is generally admitted that the human race can be divided into a number of different groups, but the question of the exact nature of these groups is still a matter of debate. Some authorities believe that the human race can be divided into a number of different groups, while others believe that it cannot. The question of the classification of the human race is one of the most important questions in anthropology, and it is one which has attracted the attention of many of the most distinguished scientists of the present day.

The fourth of the questions mentioned above is the question of the influence of the environment on the human race. It is generally admitted that the environment has a great influence on the human race, but the question of the exact nature of this influence is still a matter of debate. Some authorities believe that the environment has a great influence on the human race, while others believe that it has a small influence. The question of the influence of the environment on the human race is one of the most important questions in anthropology, and it is one which has attracted the attention of many of the most distinguished scientists of the present day.

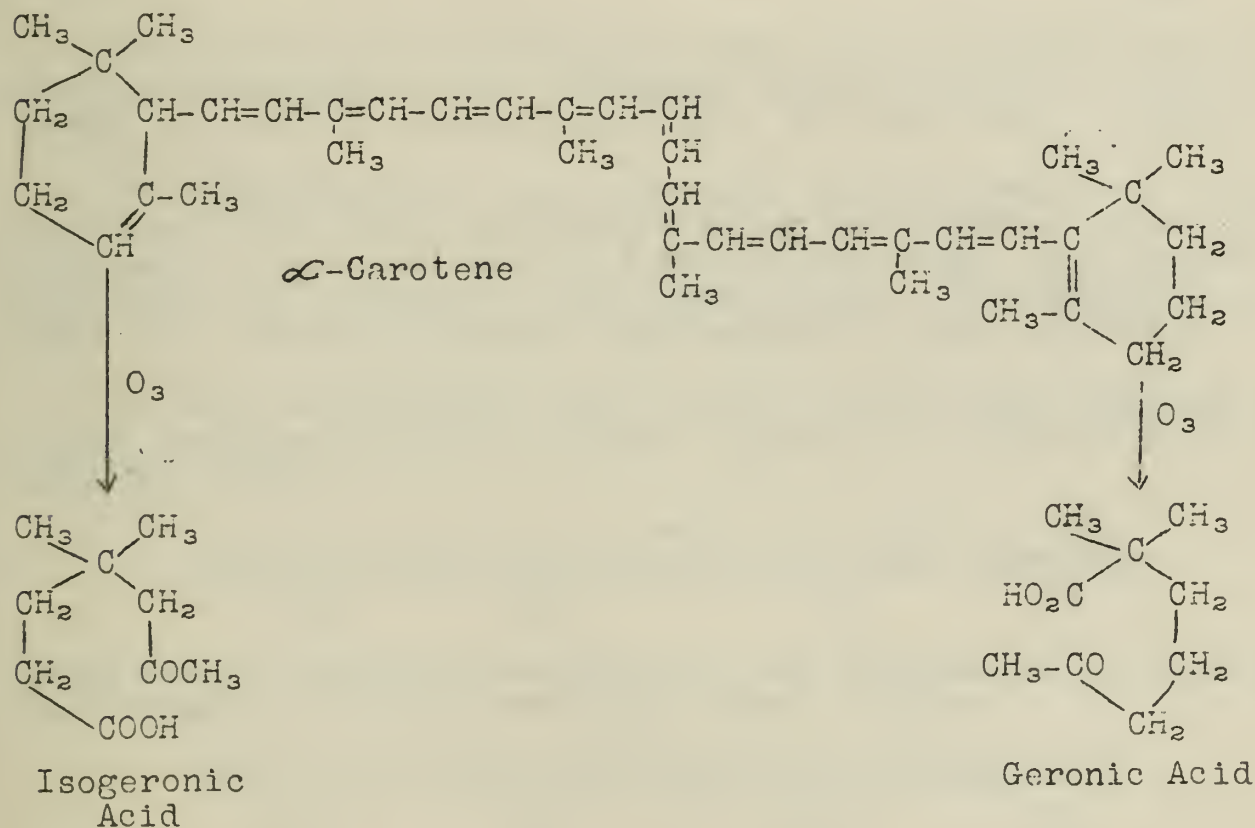
The fifth of the questions mentioned above is the question of the future of the human race. It is generally admitted that the human race has a future, but the question of the exact nature of this future is still a matter of debate. Some authorities believe that the human race has a bright future, while others believe that it has a dark future. The question of the future of the human race is one of the most important questions in anthropology, and it is one which has attracted the attention of many of the most distinguished scientists of the present day.

Karrer synthesized the reduced hydrocarbon, $C_{40}H_{82}$, from dihydrophytyl bromide through the Wurtz synthesis.

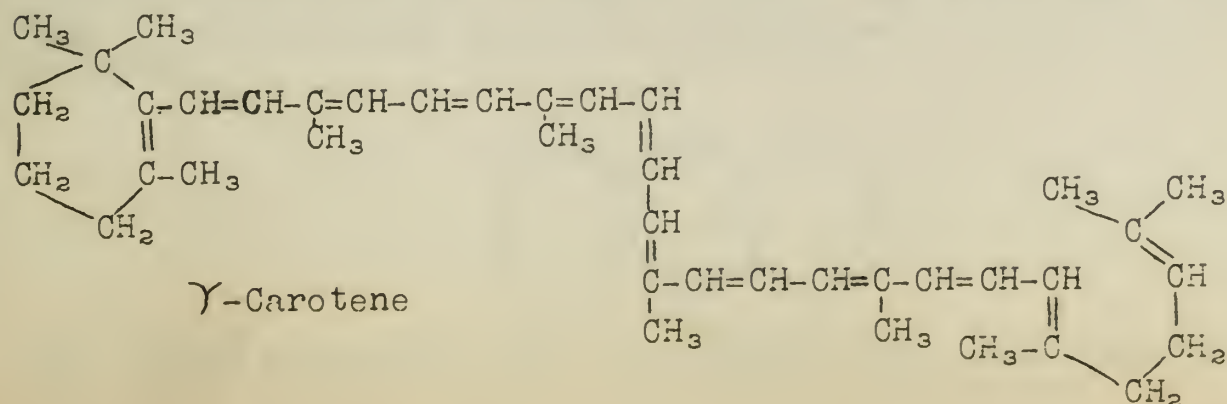
β -Carotene also gave on gentle oxidation semi- β -carotenone, β -carotenone, and β -carotene oxide. In these compounds the ring double bonds have been attacked by the reagent.

The nature of the central chain in β -carotene was also disclosed by thermal degradation. Besides toluene and m-xylene some 2,6-dimethylnaphthalene was isolated. Trans-crocetin dimethyl ester, containing no rings, on cyclization also yielded the latter product, proving the chains in the two compounds to be similar.

Oxidation of α -carotene with permanganate gave the same products which were obtained from β -carotene. Ozonization, however, gave both geronic and isogeronic acids.



γ -Carotene is an isomer having absorption maxima intermediate between the purely aliphatic lycopene and β -carotene. On ozonization it yields some acetone. The structure suggested is:

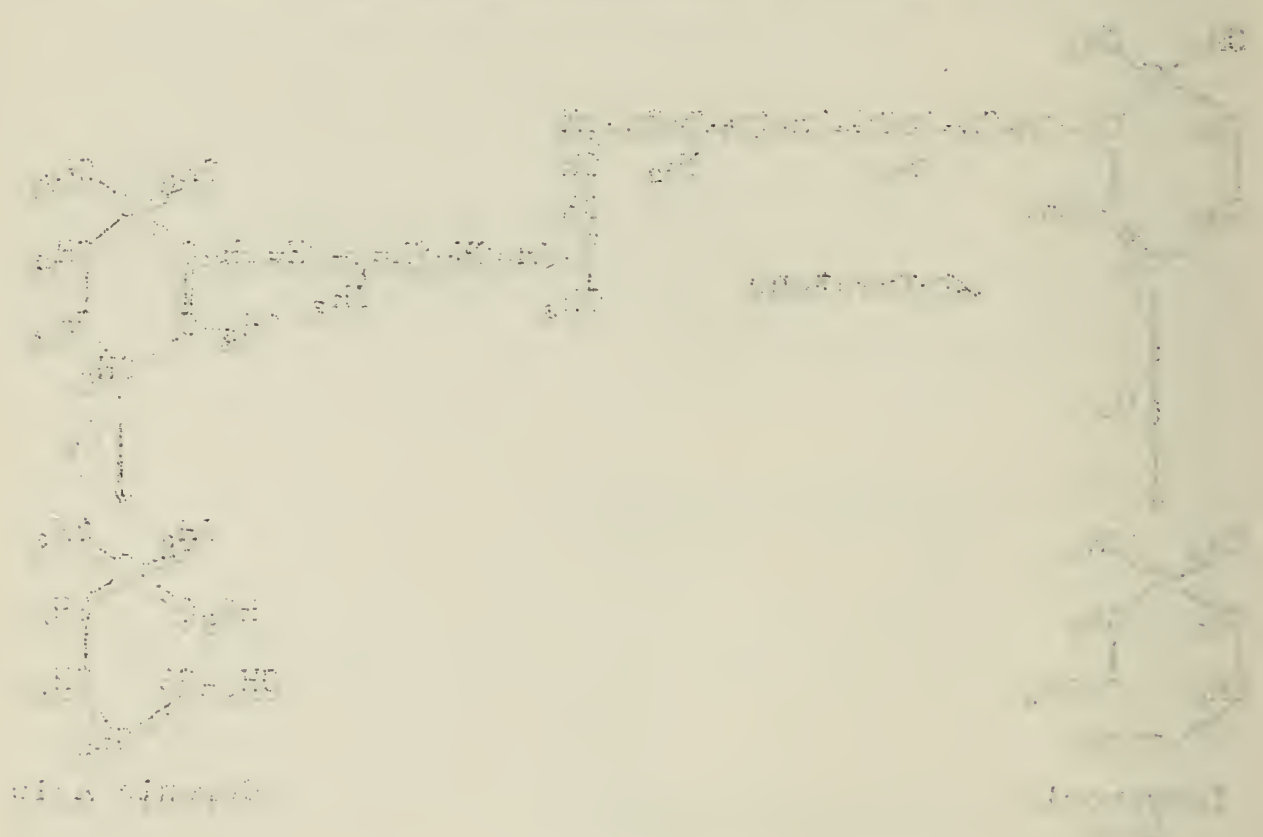


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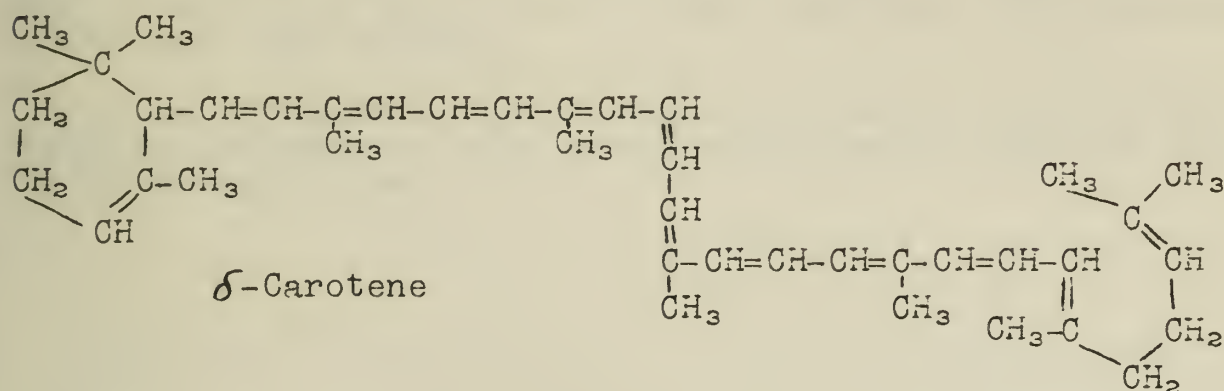
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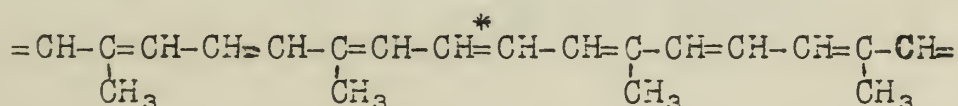
A fourth possible isomer with absorption maxima intermediate between lycopene and ϵ -carotene was reported by Winterstein in 1933. It was separated chromatographically but not in sufficient amount for analysis. The suggested structure is:



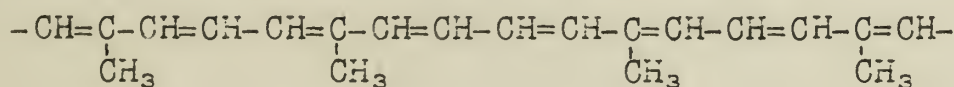
The naturally-occurring carotenes may be divided into five classes according to the functional groups present: hydrocarbons, alcohols, ketones, carboxylic acids, and carboxylic esters.

The hydrocarbons, e.g., lycopene and carotene, are considered the parent molecules, all others being derived from these by hydrogenation or ketonization of the ionone rings, curtailment of the chain, or by shift of the double bonds. The hydroxyl derivatives are commonly known as xanthophylls or phytoanthins.

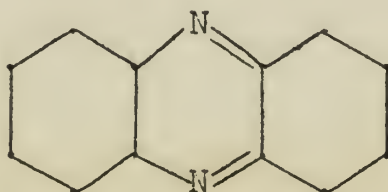
In most carotenoids there occurs a C_{20} -chain composed of two double isoprene skeletons linked together by a double bond (*) to form the system,



which may be terminally reduced by two hydrogen atoms causing the interchange of double and single bonds to give

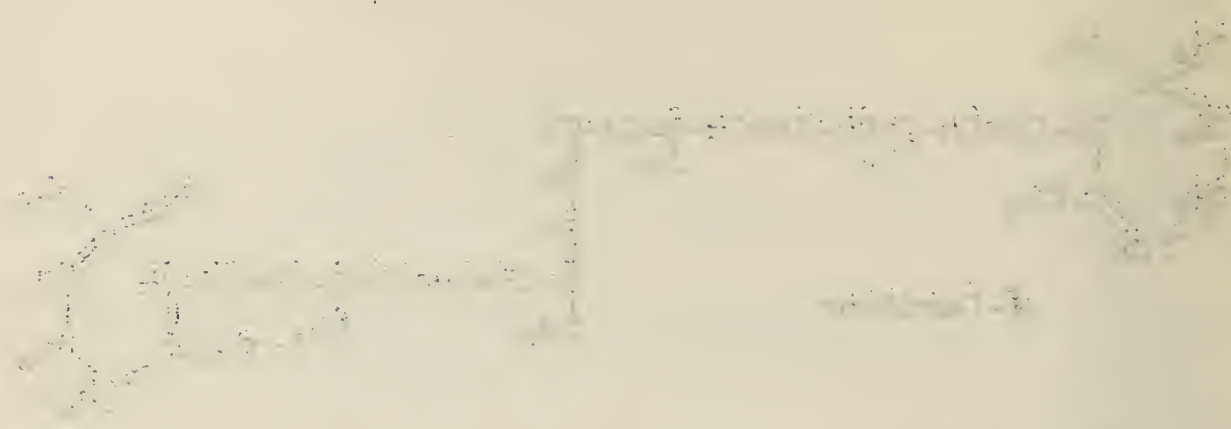


The study of pigments formed by bacteria is of considerable interest for these microorganisms can synthesize such complicated ring systems as phenagins and dipyrrolyls out of the simplest organic substances and inorganic salts. Pyocyanin and chlororaphin, whose structures have been well established, are derivatives of phenagins.



They show a remarkable ease of oxidation and reduction and may be involved in certain biochemical oxidation processes.

The following is a list of the names of the persons who have been elected to the office of Justice of the Peace for the year 1900. The names are given in alphabetical order.



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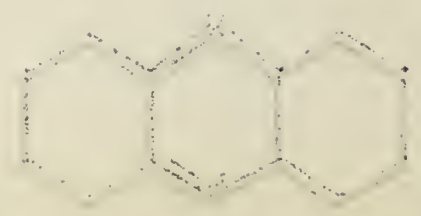
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-4-

The pigments formed by various fungi have been studied by K^ögl and his students for a number of years. Those studied have been found to be derivatives of the terphenyl, phenanthrene, and anthracene ring systems.

Some carotenoid pigments have also been isolated from bacteria by Karrer. Work on the structure of these is in progress at the present time.

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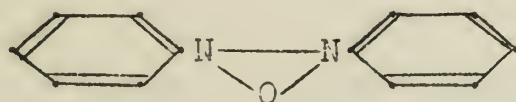
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Reported by W. J. Peppel
J. H. Van Campen
April 7, 1937.

THE AZOXY COMPOUNDS

(from Die Azoxy Verbindungen by Eugen Muller--
Ahren's Sammlung, 33 (1936))

The Determination of the Structure of Azoxy Compounds.--Azoxy benzene was first made by Zinin¹ in 1841 by reducing nitrobenzene with alcoholic KOH. He pointed out at that time that it was intermediate in the reduction of nitrobenzene to aniline. The first structural formula assigned to the compound was due to Kekulé who chose it arbitrarily and without any experimental justification whatsoever.

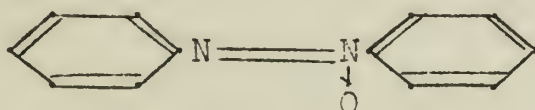


Kekulé formula

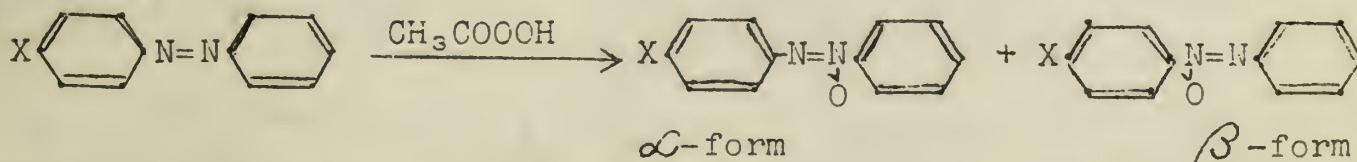
The work of Angeli (1913 et. f.) led to the formulation of the structure as it is now accepted. Angeli obtained azoxy benzene through the condensation of aniline and nitrobenzene. The similarity between this reaction and the reaction between hydroxylamine and nitrobenzene to give phenyl nitroso hydroxylamine, led him to write the structure of the resulting compound thus:



In the light of modern theory of the structure of the nitrogen atom and of valence together with evidence furnished by a comparison of parachor values this is now modified to include the semi-polar bond between the oxygen and nitrogen.



Since he had noted isomerism in the case of the phenyl nitroso hydroxyl amines, he believed that he should also be able to find it in the case of unsymmetrically substituted azoxy benzenes. Ordinary methods for the production of azoxy compounds always led to the formation of symmetrically substituted compounds. Angeli² developed the method (used even today) for the production of unsymmetrically substituted azoxy benzenes. Essentially his method is the oxidation of the corresponding azo compound with peracetic acid to the azoxy compound. The reaction is carried out in a mixture of glacial acetic acid and 30 per cent H_2O_2 .



Many compounds of this type have been prepared. It should be noted that these isomers are of the structural type and not stereoisomers, and that there should be no tendency, therefore, for them to change into the other form. Angeli found that the α -form was not susceptible toward nitration while the corresponding β -form was easily

The following is a list of the names of the members of the Royal Society of Medicine, who have been elected to the office of President for the year 1891-1892. The names are arranged in alphabetical order, and are given in full, with their degrees and titles, where applicable. The names are given in the order in which they were elected, and are not necessarily in the order of their seniority.



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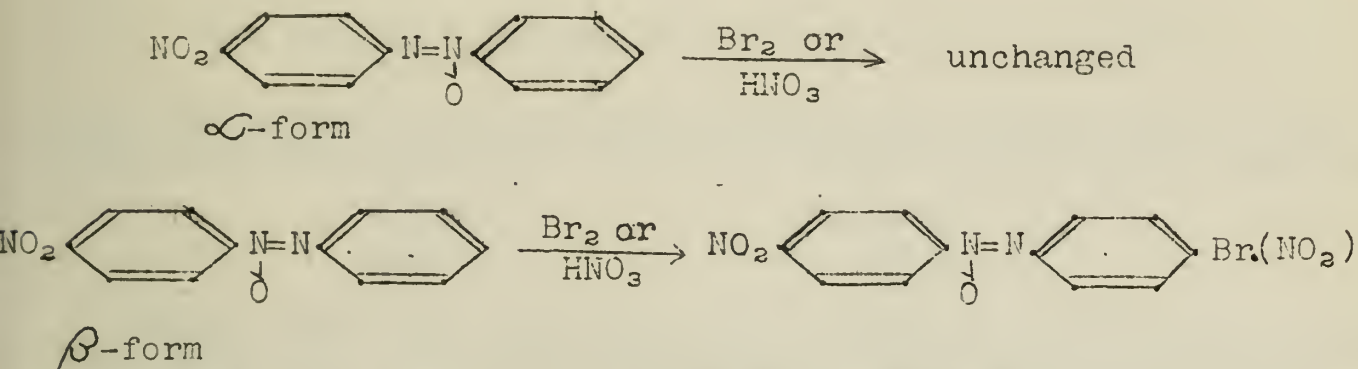


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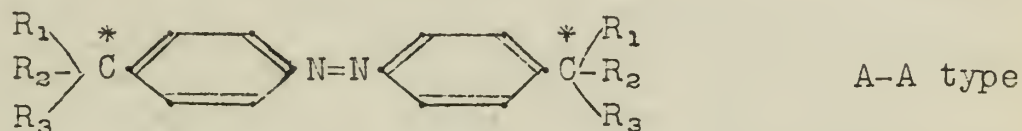


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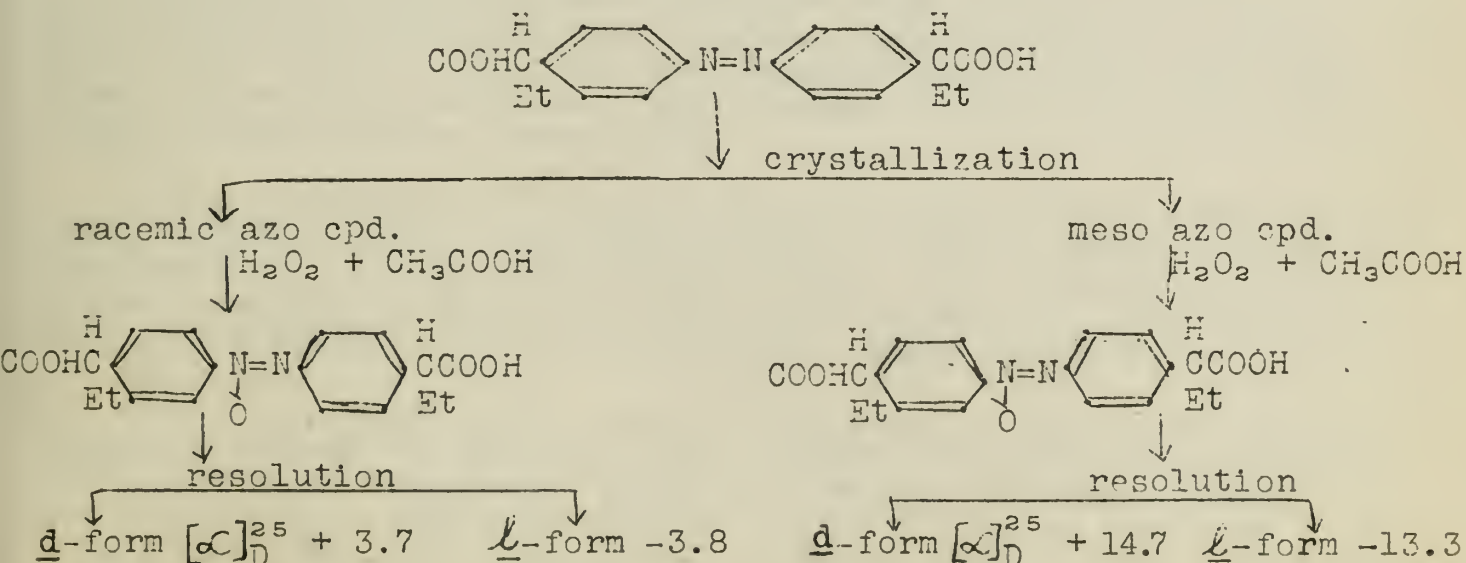
nitrated. This held true for all of the isomeric pairs studied. From analogous reactions in the series of the azo compounds, he concluded that the presence of the oxygen had a protective effect on the benzene ring to which it was adjacent. He also concluded that when substitution occurred in an unsubstituted ring, it was always in one attached to a trivalent nitrogen. He was thus led to assign the following structures to the two isomers.



The work of Marvel³ and later that of Mueller⁴ on optically active azoxy compounds furnished a new type of evidence for the unsymmetrical nature of the azoxy grouping. It has been shown that the azoxy grouping is not capable of producing molecular asymmetry by itself. However, a compound of the type



should exist in one racemic and one meso compound. Oxidation of this azo compound with peracetic acid to the azoxy compound should give two racemic modifications providing Angeli's postulations were correct. If the Kekulé formula were correct, then oxidation of the meso azo compound should give a meso azoxy compound. The compounds studied by Marvel and the forms isolated follow:



Mueller's work is essentially of the same character and his results are in full agreement with those of Marvel.

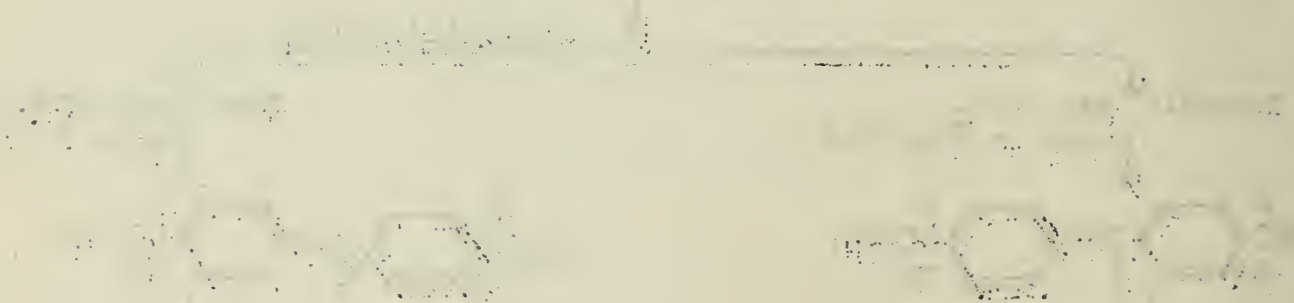
The first step in the synthesis of the polymer is the reaction of the monomer with the initiator. This reaction is exothermic and produces a radical species. The radical species then reacts with another monomer molecule, forming a dimer radical. This process continues, leading to the formation of a long polymer chain. The reaction is controlled by the concentration of the initiator and the monomer.



The polymerization process is a chain reaction. It begins with the formation of a radical species, which then reacts with monomer molecules to form a growing polymer chain. The chain continues to grow as it reacts with more monomer molecules. The process is controlled by the concentration of the initiator and the monomer.



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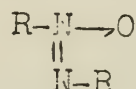
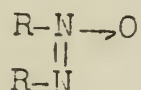


The polymerization process is a chain reaction. It begins with the formation of a radical species, which then reacts with monomer molecules to form a growing polymer chain. The chain continues to grow as it reacts with more monomer molecules. The process is controlled by the concentration of the initiator and the monomer.

Other methods which have served to distinguish between the two proposed structures include comparisons of molecular refractivity, adsorption spectra, and the parachor. In all cases there is little doubt that the original formulation of Angeli agrees much better with the experimental evidence, and there is no doubt as to the unsymmetrical nature of the azoxy compounds.

The Spatial Configuration of the Azoxy Compounds

The presence of a nitrogen-to-nitrogen double bond in the azoxy compounds suggests the possibility of cis-trans isomerism:



This idea was first expressed by Hantsch and Werner in 1890. Since that time the stereoisomerism of the azoxy compounds has often been the object of much investigation and discussion. However, all of the earlier allegedly prepared isomers with the exception of those of Reissert have lacked confirmation by later researches.

Reissert, thinking that the possible isomers of azoxybenzene might be stable only at low temperatures, investigated the action of a water-alcohol solution of sodium hydroxide on nitrosobenzene and on *o*-nitrosotoluene at 0° C. He was able to obtain small amounts of higher melting isomeric forms, which upon slight warming were transformed into the ordinary known compound. His work offered nothing conclusive on the existence of stereoisomerism in these compounds.

Recently Müller and Kreutzmann have repeated Reissert's experiments. They were able not only to obtain the isomeric forms of azoxybenzene and *o,o'*-azoxytoluene reported by Reissert, but upon further experimentation obtained those of *o*-azoxyanisole, *o,o'*-dichloroazoxybenzene and others. Using Reissert's method they found that, in general, the isomers could be obtained only when *o*-substituted nitroso-compounds were used, the *p*-compounds always producing the normal form.

Later, starting with hydroxylamine- and nitroso-compounds and using aqueous alkali and dioxan as the solvent, they were able to prepare the *p*- and *m*-substituted isomers, thus showing that the stereoisomerism of the azoxy compounds is general, including not only the unsubstituted but the *o*-, *m*-, and *p*-compounds as well.

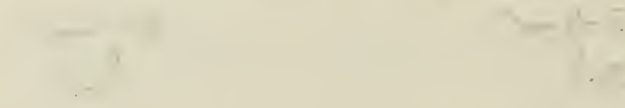
The various isomeric forms (known also as iso-azoxy compounds) obtained to date are less soluble than the corresponding normal forms in the usual organic solvents. They have higher melting points. The melting point of an isomer is also its transition point into the normal compound. The colors of the compounds are almost identical, being usually faintly greenish-yellow or colorless.

The elucidation of the structure and spatial configuration

Other well-known names were mentioned in connection with the
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THE HISTORY OF THE CITY OF NEW YORK

The history of the city of New York is a subject of great interest
and importance to the people of the city and to the world.



The city of New York is one of the most important cities in the world
and has a long and interesting history. It was first settled by the
Dutch in 1624 and was then known as New Amsterdam. It was later
taken over by the English in 1664 and was then known as New York.

The city of New York has a rich and varied history. It has been the
center of many important events in the history of the United States.
It has been the site of many important battles and has played a
major role in the development of the country.

The city of New York is a city of many firsts. It was the first
city to be founded by a group of people who were not from the
British Isles. It was the first city to be founded by a group of
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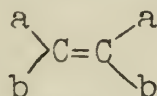
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of these new compounds is best obtained from the study of various physical properties. Of these, three are especially suitable:

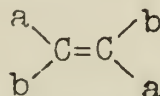
1. Ultraviolet light absorption spectra. It is known that the ultraviolet absorption spectra of cis-trans isomers of the $-C=C-$ type and of the syn- and anti-diazo cyanides are very similar. This is also found to be true of these isomeric azoxy compounds.

2. The spectrochemical behavior of the compounds.

3. The determination of dipole moments. In compounds of the type



and



the trans-form shows a dipole moment $M=0$, since like groups are located opposite to each other through the center of the molecule. The cis-form on the other hand always possesses a moment $M>0$.

This is found to be true of the azoxy compounds excepting that the trans-form, due to the presence of the $-N-\underset{\text{O}}{N}-$ group, also possesses a finite moment greater than 0 but smaller than that of the cis-isomer.

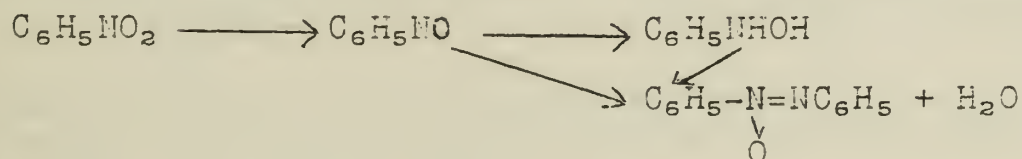
Preparation of the Azoxy Compounds

There are three methods of preparing azoxy compounds:

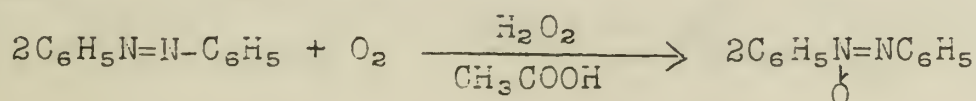
1. Condensation of hydroxylamines and nitroso-compounds:



2. Reduction of nitro-compounds:



3. Oxidation of the corresponding azo compounds:



Bis- and Polyazoxy Compounds

Under special conditions it is possible to prepare compounds possessing more than one azoxy group. The following three isomeric bis-azoxy compounds have been prepared:

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- | | |
|---|------------|
| 1. $\text{C}_6\text{H}_5\text{N}=\text{N}-\text{C}_6\text{H}_4-\text{N}=\text{N}-\text{C}_6\text{H}_5$
<div style="display: flex; justify-content: space-around; width: 100%;"> <div style="text-align: center;">\downarrow
O</div> <div style="text-align: center;">\downarrow
O</div> </div> | M. P. 168° |
| 2. $\text{C}_6\text{H}_5\text{N}=\text{N}-\text{C}_6\text{H}_4-\text{N}=\text{N}-\text{C}_6\text{H}_5$
<div style="display: flex; justify-content: space-around; width: 100%;"> <div style="text-align: center;">\downarrow
O</div> <div style="text-align: center;">\downarrow
O</div> </div> | M. P. 148° |
| 3. $\text{C}_6\text{H}_5\text{N}=\text{N}-\text{C}_6\text{H}_4-\text{N}=\text{N}-\text{C}_6\text{H}_5$
<div style="display: flex; justify-content: space-around; width: 100%;"> <div style="text-align: center;">\downarrow
O</div> <div style="text-align: center;">\downarrow
O</div> </div> | M. P. 153° |

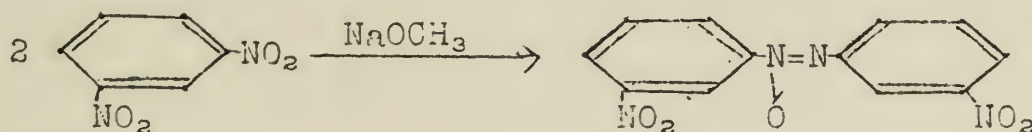
Likewise there are four possible ~~tris~~-azoxy compounds. Closed-ring azoxy compounds are also known.

Reactions of the Azoxy Compounds

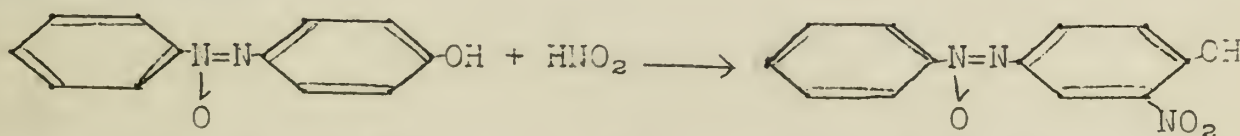
1. Oxidation.--The azoxy compounds are in general very resistant to oxidizing agents. Azoxy phenols, however, are readily attacked by alkaline permanganate solutions.

2. Reduction.--In acid medium, azoxy compounds are easily reduced directly to the amines. In alkaline medium, using mild reducing agents bimolecular reduction occurs, and from azoxybenzene, for example, one obtains successively, azobenzene, hydrazobenzene, and aniline.

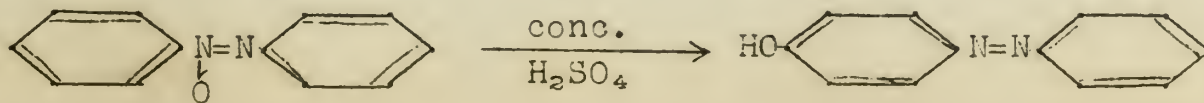
3. Nitration.--The introduction of a nitro group into the benzene ring of an azoxy compound can occur in three ways, (1) the starting material may be nitrated in the proper position in the ring and the compound then reduced. Thus, starting with 1,3-dinitrobenzene one obtains 3,3'-dinitroazoxybenzene:



(2) Direct nitration of the azoxy compound with concentrated nitric acid. (3) Direct introduction of the nitro group into the ring by means of nitrous acid:



4. Wallach's Transformation.--Upon heating with concentrated sulfuric acid, the azoxy compounds undergo a peculiar intermolecular rearrangement, whereby the azoxy oxygen migrates to one of the benzene rings thus forming an hydroxy-azo-compound.



1. 1,2,3,4-tetrahydronaphthalene
2. 1,2,3,4-tetrahydronaphthalene
3. 1,2,3,4-tetrahydronaphthalene

These three are the only tetrahydronaphthalenes which are known to occur in nature.

1,2,3,4-Tetrahydronaphthalene

This is the most common of the tetrahydronaphthalenes. It is a colorless, odorless liquid, boiling at 190°C. It is soluble in most organic solvents.

It is formed by the hydrogenation of naphthalene. The reaction is reversible, and the equilibrium lies to the right. It is also formed by the hydrogenation of 1,2,3,4-tetrahydronaphthalene.

It is a very important compound in the chemical industry. It is used as a solvent and as a starting material for the synthesis of many other compounds.



It is also known as tetralin. It is a very important compound in the chemical industry. It is used as a solvent and as a starting material for the synthesis of many other compounds.



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5. Effect of Light.--The action of light on the azoxy compounds leads to the same final products as the treatment with concentrated sulfuric acid.

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Reported by L. S. Keyser
A. J. Johanson
April 14, 1937.

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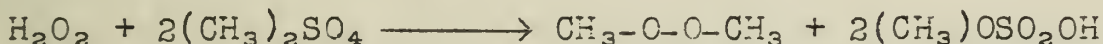
The Preparation and Properties of the Most Important Types of Peroxides

1. Alkyl Hydroperoxides: ROOH



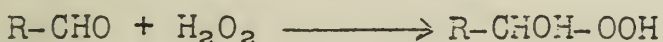
Methyl hydroperoxide is a very explosive liquid. Higher alkyl homologs are successively less explosive. The oxidizing action of these peroxides is less than that of H_2O_2 .

2. Dialkyl Peroxides: R-O-O-R



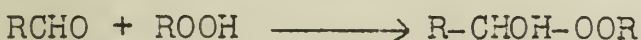
Dimethyl peroxide is a liquid which is very sensitive to shock. The higher homologs are progressively more stable. Dimethyl peroxide decomposes into CH_3OH and HCHO , higher homologs are catalytically decomposed by FeSO_4 to the corresponding alcohols and aldehydes. The oxidizing action of these peroxides is very weak.

3. Hydroxy Alkyl Hydroperoxides: R-CHOH-OOH



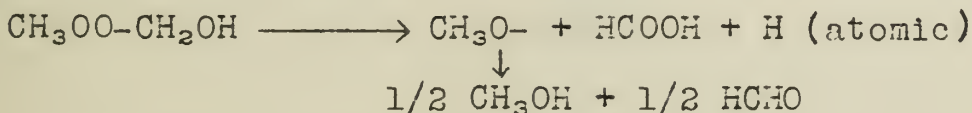
Hydroxy ethyl hydroperoxide is found in autooxidized ether. The compounds formed by lower aldehydes are liquid; those from higher aldehydes are solid compounds.

4. Hydroxy Dialkyl Peroxides: R-CHOH-OOR



Hydroxy dialkyl peroxides are distillable liquids which are as stable as hemiacetals.

Hydroxy dimethyl peroxide decomposes with alkali as follows:



5. Diacyl Peroxides: R-CO-OO-CO-R



The only peroxide as yet prepared on an industrial scale, benzoyl peroxide, occurs in this group. It is used in bleaching fats, flour, and meal, and especially as a catalyst for the polymerization of unsaturated compounds. These compounds decompose violently only if heated.

6. Per Acids: R-CO-OOH



Per acids are rather unstable. As in the other types of

peroxides the lower members are explosive, the higher members more stable. They catalyze polymerization reactions, and are most important, practically, for the analytical determination of double bonds.

The Theories Concerning Autooxidation Processes

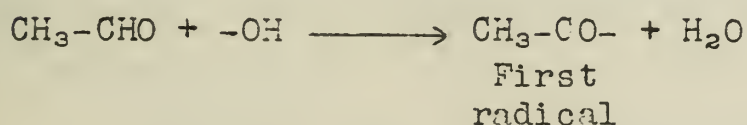
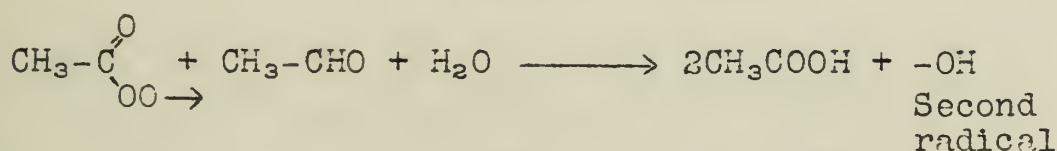
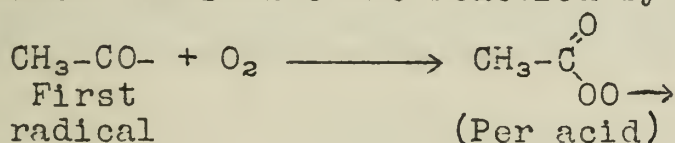
In Which Peroxides are the Intermediate or End Products

The three theories that have received most attention are those of Manchot, Wieland, and Willstätter. All consider that the ferrous ion may act as a catalyst.

Manchot believes that a peroxide Fe_2O_5 is formed and transfers the oxygen to the substrate, itself being reduced again to the ferrous state, the process being repeated.

Wieland supposes that ferrous iron forms a complex with the substrate in which the hydrogen atoms are activated. An atom of ferrous iron is capable of adding to many substrate molecules, thus perpetuating the process.

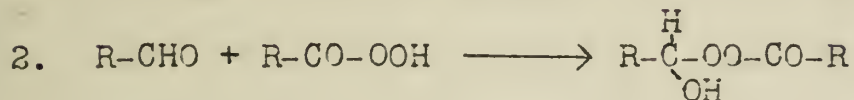
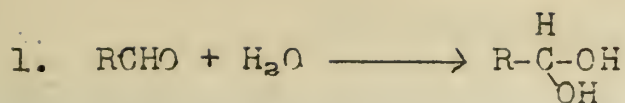
Willstätter postulates a chain reaction in which radicals result from the influence of the catalyst or of light. Willstätter and Haber illustrate the reaction by the following scheme:



The Oxidation of Compounds with the >C=O Group

The autooxidation of aldehydes and ketones is influenced markedly by the presence of metal salts and by light. The researches of Kuhn and Wieland show that the oxidation of aldehydes in organic solvents or in water solution requires iron. Completely iron-free benzaldehyde in solution would not oxidize when exposed to air; in the presence of a trace of iron there was rapid oxidation. Pure benzaldehyde itself will oxidize in the iron-free state.

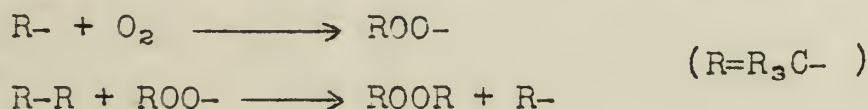
Per acids are formed as intermediates in the oxidation of aldehydes and can be isolated. They can react with the unchanged aldehyde in various ways:



The Oxidation of Unsaturated Hydrocarbons

Simple olefins such as ethylene and its homologs do not form peroxides readily. Terpenes and compounds such as cyclohexene readily form peroxides. The polymerization or resinification of gasoline and lubricating oils is thought to be due to peroxide formation, as is the drying of oils.

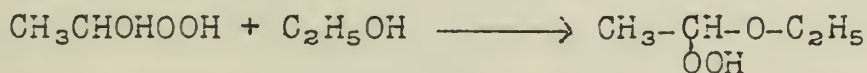
Dissociated ethanes such as hexaphenyl ethane are oxidized in solution more rapidly than they dissociate. According to Zeigler and Orth this can be explained by the following mechanism:



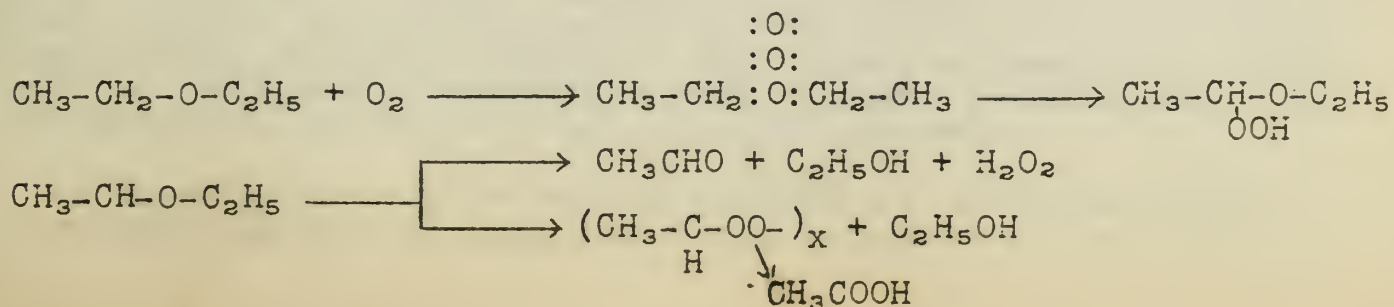
In general such carbon-carbon double bonds as are strongly affected by unsaturated groups in the vicinity add oxygen readily.

Autooxidation of Ethers

It has been shown that in autooxidized ether there is present H_2O_2 , ethyl alcohol, acetic acid, acetaldehyde, and an ether peroxide. The latter behaves similarly to ethylidene peroxide, a polymeric peroxide. Clover believed this peroxide to be $\text{CH}_3-\underset{\text{OOH}}{\text{CH}}-\text{O}-\text{C}_2\text{H}_5$. Reiche synthesized this peroxide by the following series of reactions:

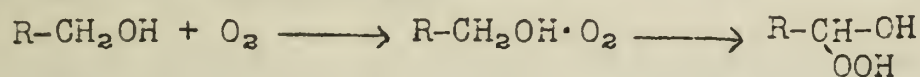
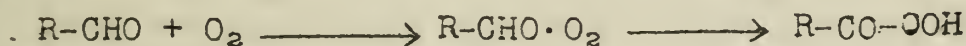
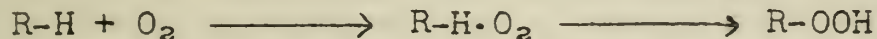


This peroxide was found to give on cleavage the products present in autooxidized ether. Upon heating the peroxide the polymeric ethylidene peroxide is formed. The following scheme represents the entire process:



The Mechanism of Oxidation

The mechanism of oxidation is probably an insertion of an oxygen molecule between a C and the H according to the relations:



Applications

Rancidity of fats is not caused by saponification, but is rather due to an oxidative decomposition of the unsaturated acid esters to simpler acids of disagreeable odor. This decomposition may be arrested by the usual antioxidants, by the presence of a few naturally-occurring dyestuffs, and by temperature control and exclusion of bacterial action.

In this connection, oxygen may react with both an active methylene and a double bond. Unsaturated hydrocarbons with active methylene groups may be oxidized to α - β unsaturated ketones. Double bond reaction is shown by monomeric ethylene peroxides which are comparable to molozonides, whose structure were confirmed by optical means and by actual synthesis of an azonide without using ozone.

The drying of oils is a simultaneous polymerization and oxidative decomposition. The polymerization process, in general produces a more desirable film. The nature of the pigment widely influences the behavior. The esters of the unsaturated acids are decomposed by oxygen in the drying process; peroxides are doubtless intermediates in the process.

The mechanisms of oxidation of fuel gas-air mixtures, the bleaching of dyes, digestion of food by animal organisms are generally agreed to include peroxide intermediates.

Photo-oxidation in light is caused by active oxygen. Chlorophyll and fluorescent dyes, for example, have been observed to oxidize solutions of ferrous salts. There are two methods of photo-oxidation: that with compounds of two valences providing reduction and autooxidation, and that of light oxidation in the presence of sensitizers.

The assimilation of green plants in light is the converse of photo-oxidation in light. According to Baeyer, CO_2 reacts with water to form formaldehyde which in turn polymerizes to starch, oxygen being the other product. Most likely a peroxidase enzyme and also organic peroxides take part in plant assimilation. The literature in the field is as yet highly polemical.

Polymerization may be caused by light or catalysts such as peroxides. Either of these may serve to activate a molecule or

The Importance of Education

The importance of education is widely recognized as a key factor in the development of a nation. It is the foundation upon which a society can build its future.

- 1. Education is the key to economic growth and development.
- 2. It is the only way to ensure that all citizens have access to the same opportunities.
- 3. Education is the only way to ensure that all citizens are able to participate in the democratic process.

Conclusion

In conclusion, education is the most important factor in the development of a nation. It is the foundation upon which a society can build its future. Without education, a nation cannot progress. Education is the only way to ensure that all citizens have access to the same opportunities. Education is the only way to ensure that all citizens are able to participate in the democratic process.

In this country, we have a long history of education. We have a long history of building a better future for ourselves and for our children. We have a long history of ensuring that all citizens have access to the same opportunities. We have a long history of ensuring that all citizens are able to participate in the democratic process. Education is the key to economic growth and development. It is the only way to ensure that all citizens have access to the same opportunities. Education is the only way to ensure that all citizens are able to participate in the democratic process.

The future of our country is in the hands of our children. We must ensure that they have the best possible education. We must ensure that they have access to the same opportunities as we did. We must ensure that they are able to participate in the democratic process. Education is the key to economic growth and development. It is the only way to ensure that all citizens have access to the same opportunities. Education is the only way to ensure that all citizens are able to participate in the democratic process.

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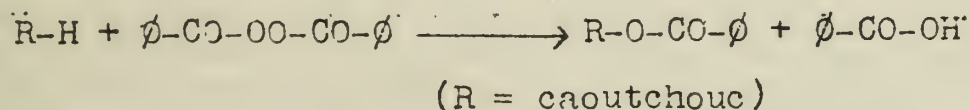
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group which in turn initiates a chain of varying length. Activation by light has been attributed to formation of active oxygen, which in turn adds to a double bond to form an organic peroxide. The peroxide, once formed, may act as a dehydrogenating agent for the alkyl adjacent, which appears to be the case in polymerization by light.

Vulcanization of caoutchouc with benzoyl peroxides was found not to change the number of double bonds. From evidence that one-half the benzoyl peroxide resulted as benzoic acid, Pummerer concludes the following reaction:



Some polymerization doubtless occurs simultaneously.

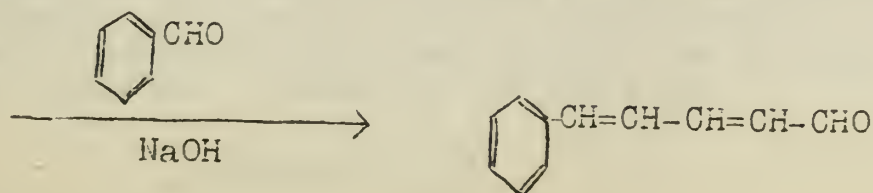
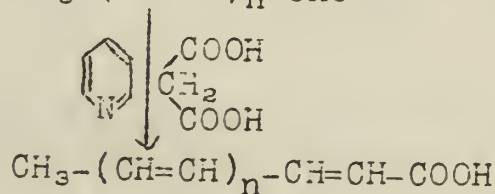
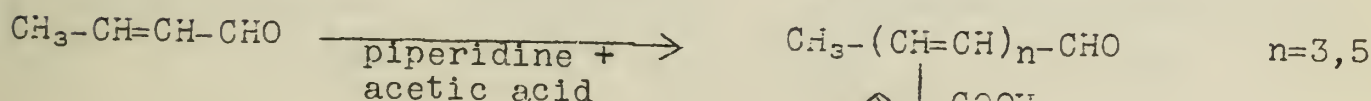
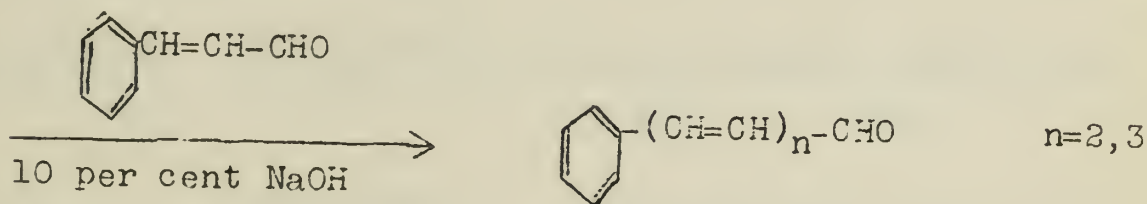
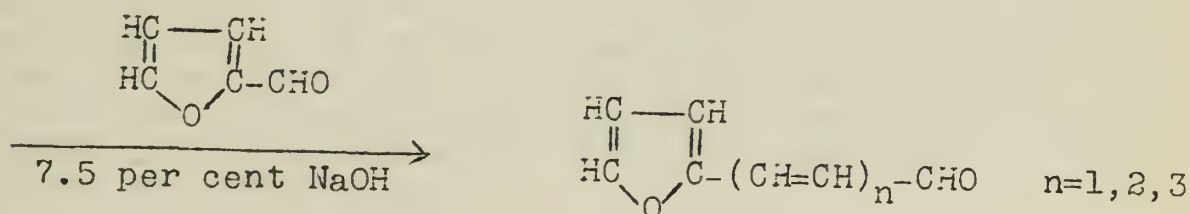
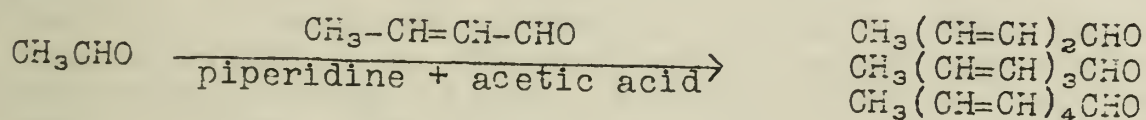
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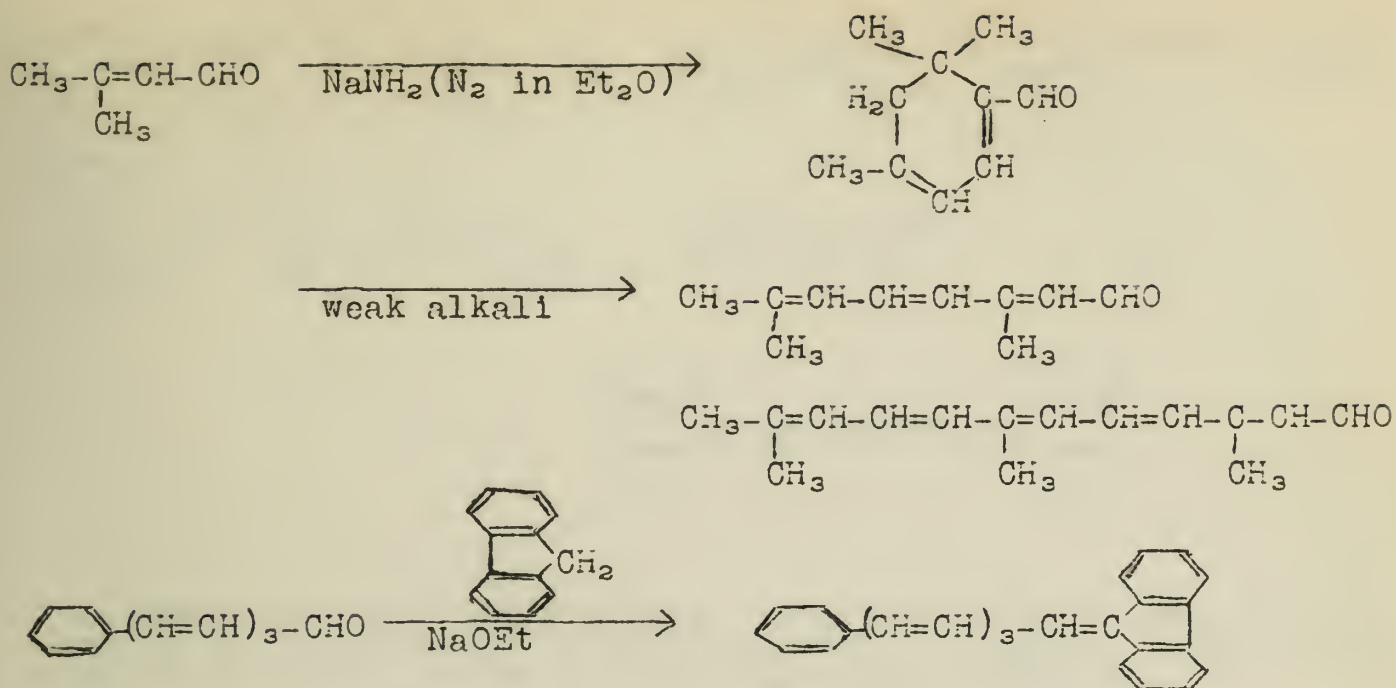
Reported by S. Jack Davis
C. H. McBurney
April 21, 1937.

THE SYNTHESIS OF POLYVINYLENE CHAINS

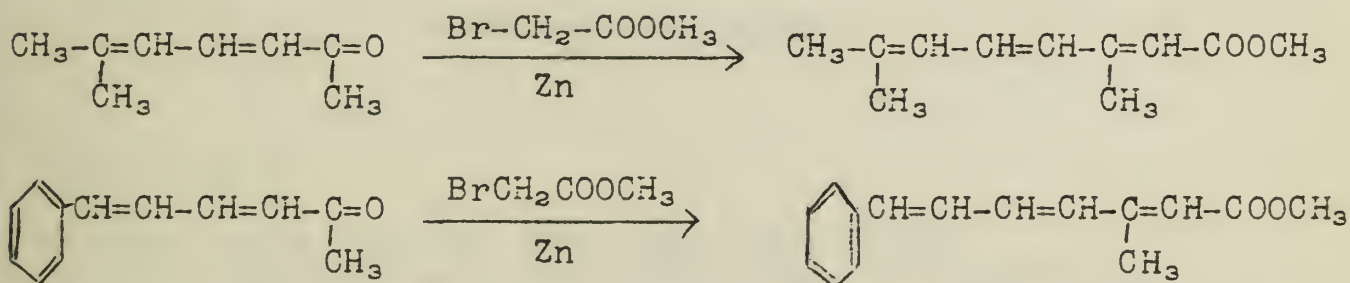
Knoevenagel Reaction.--This reaction is probably the most general one for the synthesis of polyvinylene compounds. It has been used to prepare conjugated unsaturated chains up to fourteen carbon atoms, *ω*-phenyl polyenes and a few cyclic aldehydes. The reaction is commonly catalyzed by secondary amines: however, the active agent is not the free amine, but the amine salt or substituted ammonium ion. It appears that the advantage of secondary amines over primary amines rests in the greater basicity of the former. Piperidine has been found most satisfactory as a catalyst, though diethylamine and dimethylamine have been used. Most other amines have been found to give unsatisfactory results. The reaction is carried out by adding a small amount of piperidine in an excess of acetic acid to the aldehyde with moderate heating. The reaction mixture or its ether extract is then fractionally distilled under vacuum. The reaction is accompanied by some cyclization. Dilute solutions of sodium hydroxide may be used to catalyze the reaction of aldehydes with an active methylene group in alcoholic solution at room temperature. The reaction product is acidified, extracted and distilled under vacuum. A similar procedure is used when sodium ethoxide is employed as a catalyst.



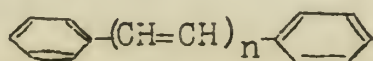
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Reformatsky Reaction.--This reaction has been used to form conjugated unsaturated esters and acids from unsaturated aldehydes and methyl ketones. The reaction is carried out in an anhydrous solvent by allowing the aldehyde or ketone to react with bromoacetic ester and zinc. The mixture is heated under reflux for fifteen minutes with aliphatic ketones or two to three hours with aromatic ketones. The reaction product is decomposed with water, acidified and distilled. If water is not split out by distillation at atmospheric pressure, the compound is dehydrated with phosphorus pentoxide and the fractions separated by vacuum distillation. This method has been used by Karrer in attempting to synthesize vitamin A from β -ionone. It is a convenient method for extending a carotinoid chain by two carbon atoms.



Kuhn's Modification of the Perkin Reaction.--This reaction has been used by Kuhn in the synthesis of a series of diphenyl polyenes. The reaction consists of the combination of two molecules of aldehyde with a molecule of succinic acid or dihydromuconic acid in the presence of acetic anhydride and lead oxide. On cooling, the diphenyl polyene separates. Compounds of the type,



have been synthesized up to $n=8$.

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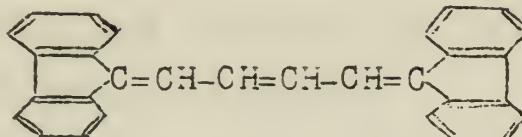
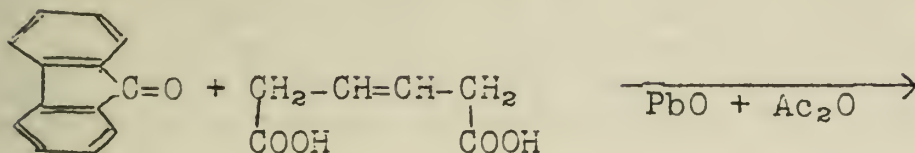
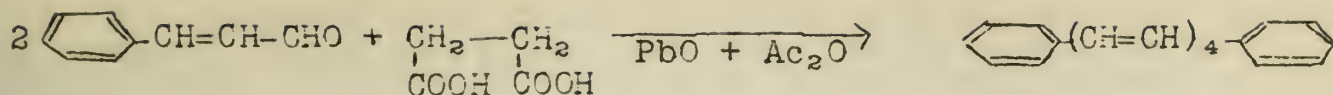
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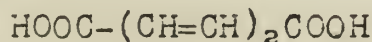
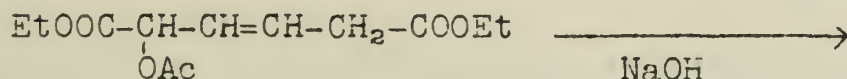
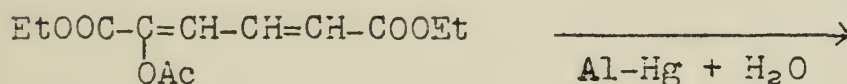
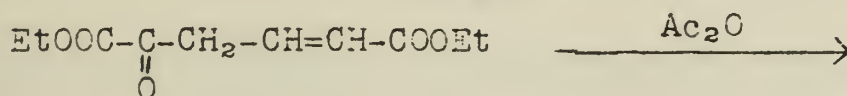
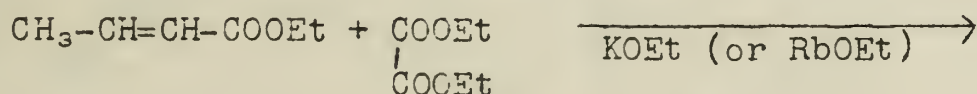
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Ethyl Oxalate Condensations.--This method has been used by Kuhn in the preparation of ω, ω' -dicarboxy polyenes. Acids of the type $\text{HOOC}-(\text{CH=CH})_n\text{-COOH}$ up to $n=5$ have been prepared.



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 Kuhn and Winterstein, *Helv. Chim. Acta*, 11, 116 (1928)
 Kuhn and Hoffer, *Ber.*, 65, 651 (1932)
 Kuhn et al, *ibid.*, 69, 98, 1757 and 1979 (1936)
 Bernhauer and Drobneck, *Biochem. Ztschr.*, 266, 197 (1933)

1. The first part of the paper is devoted to a general discussion of the problem.

2. In the second part, we shall consider the case of a single particle.

3. The third part is devoted to the case of a system of particles.

4. The fourth part is devoted to the case of a system of particles, and the fifth part to the case of a system of particles.

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5. The sixth part is devoted to the case of a system of particles.

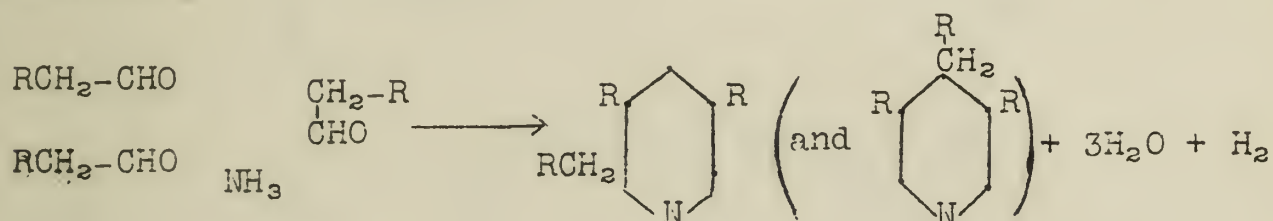
6. The seventh part is devoted to the case of a system of particles.

7. The eighth part is devoted to the case of a system of particles, and the ninth part to the case of a system of particles.

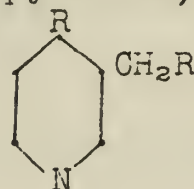
The chemistry of pyridine resembles very closely the chemistry of benzene. Pyridine is very resistant to oxidation and to direct substitution. The pyridine nitrogen directs substituents to the β positions (corresponding to meta-direction exhibited by a strongly negative group in the benzene ring). A group substituted in the α or γ position exhibits relatively great reactivity. Rapid progress has resulted largely from recent discoveries of methods of synthesis of derivatives. Illustrations follow.

Synthesis of Pyridine and its Homologs from Aldehydes, Ketones and Ammonia

Durkoff discovered the method and Tchitchibabin found that oxides of tri- and tetravalent metals were catalysts which made it possible to avoid sealed tube technic. Ammonium salts are also catalysts.

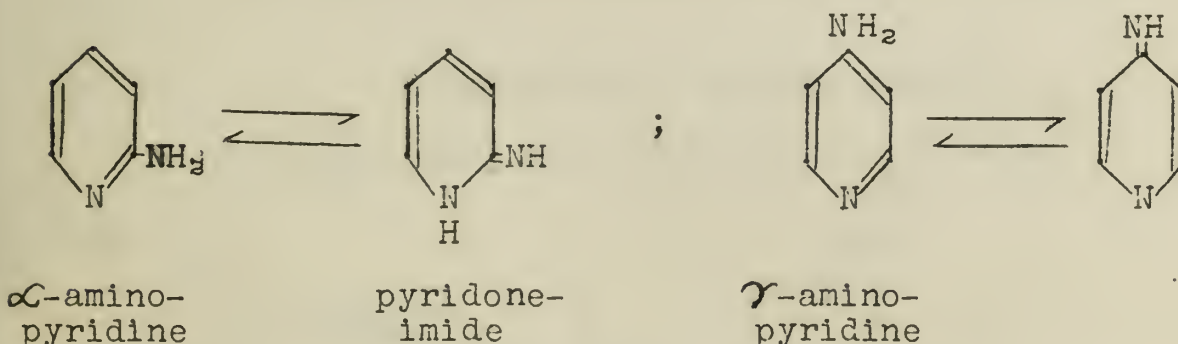


Acrolein, acetaldehyde and ammonia give pyridine; two moles of α , β unsaturated aldehyde and ammonia give



A combination of different aldehydes or different ketones or a mixture of aldehydes and ketones yield pyridine bases of varying types.

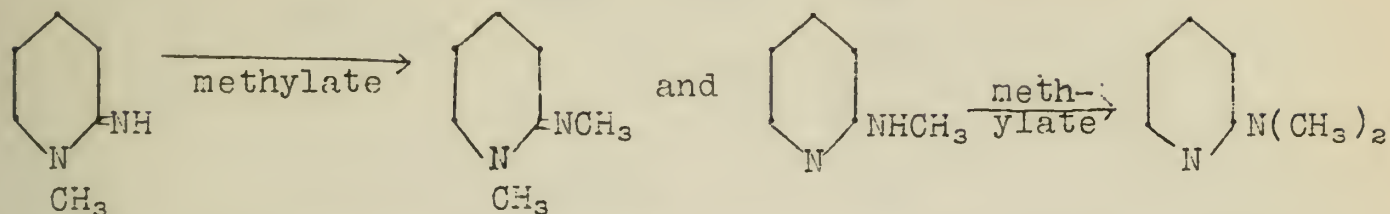
Tautomerism of α - and γ -Substituted Pyridines



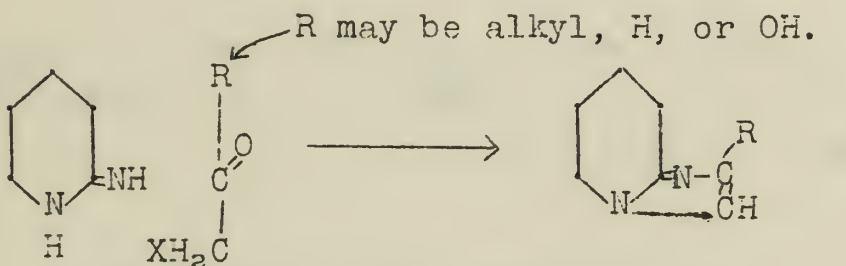
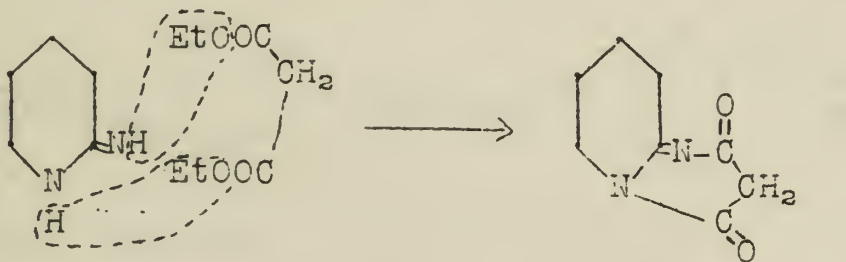
Analogous tautomers are obtained with α - or γ -hydroxypyridines and methyl pyridines. Although the tautomers have never been isolated and identified as such, their derivatives are well known. Thus, (1) O- and N-alkyl derivatives of the hydroxypyridines are obtained,

-2-

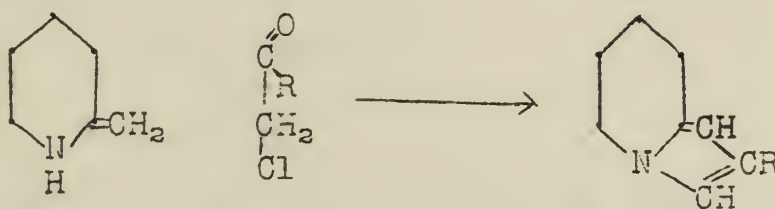
(2) methylation of α -aminopyridine proceeds in two ways



(3) cyclic derivatives of the α -aminopyridines are obtained



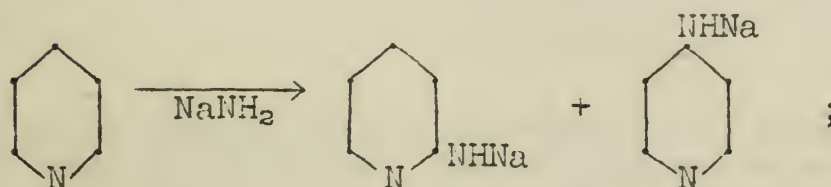
(4) cyclic derivatives of α -methylpyridines are obtained with chloroaldehydes and chloroketones



Preparation of Aminopyridines

(1) Tchitchibabin, (2) Koenigs, (3) Binz.

(1)



121. *Phenylacetylene* (C₁₀H₈) is a colorless liquid, b.p. 102°C.



122. *Phenylacetylene* (C₁₀H₈) is a colorless liquid, b.p. 102°C.



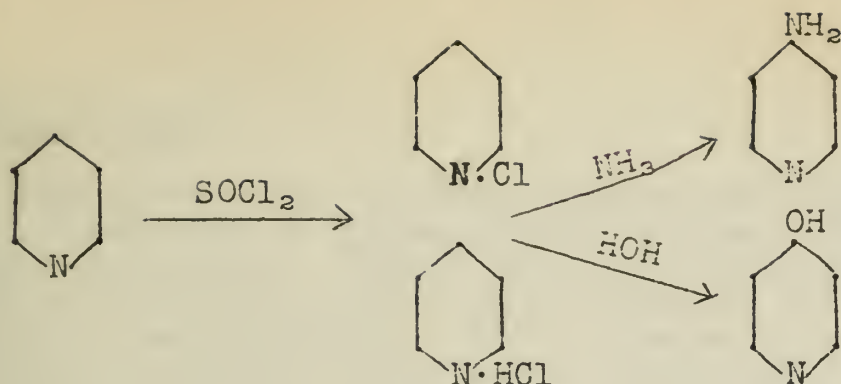
123. *Phenylacetylene* (C₁₀H₈) is a colorless liquid, b.p. 102°C.



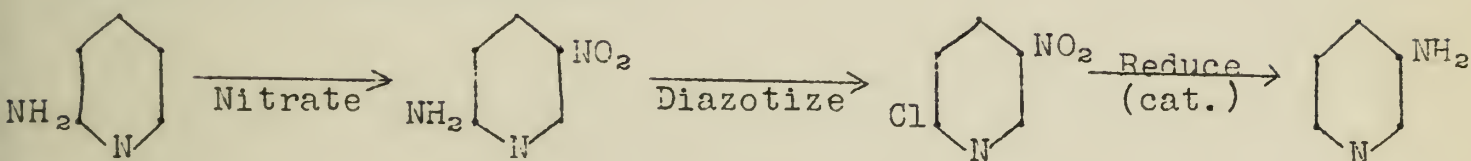
124. *Phenylacetylene* (C₁₀H₈) is a colorless liquid, b.p. 102°C.



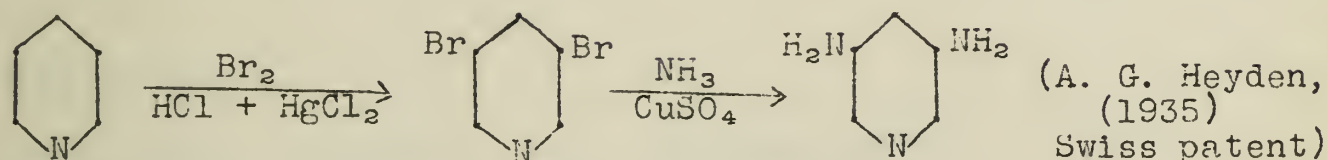
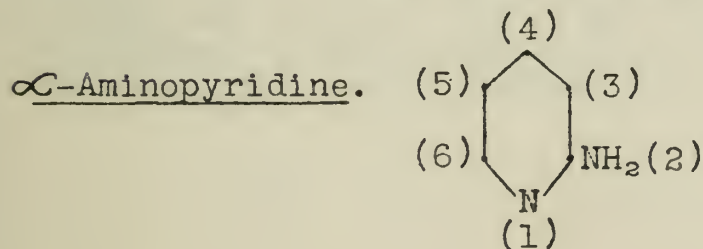
(2)



(3)



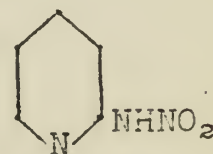
An interesting reaction:

(A. G. Heyden,
(1935)
Swiss patent)Reactions of the Aminopyridines

(a) Halogenation proceeds very readily to yield first the 5-chloro-2-aminopyridine and then the 3,5-dichloro derivative.

(b) Sulfonation and arsination (with H_3AsO_4) give mainly 2-amino-5-sulfonic and 2-amino-5-arsonic derivatives respectively.

(c) The first product of nitration is the nitramine



which on heating with concentrated H_2SO_4 rearranges to the 5-nitro and 3-nitro derivatives. The nitramine on reduction yields a hydrazine derivative which with HNO_2 gives a tetrazole derivative. The 3-nitro-2-aminopyridine on reduction and diazotization gives 2-amino-3-diazonium derivative. The α- and γ-diazonium pyridines form azo dyes with aromatic amines, phenols and aminopyridines. The latter class of azo dyes and their arsenic analogs show promise as important therapeutic agents.

β -Aminopyridine.

Substitution of the β -aminopyridines takes place much less readily than that of the α -aminopyridines. Substituents enter the 2- and 6-positions. Direct iodination has been unsuccessful. Direct chlorination with nascent chlorine gives a good yield of 2-chloro-3-aminopyridine. This compound is an important intermediate on account of the higher reactivity of the amino group and lability of the chlorine. Diazotization (very much like that of aromatic amines) proceeds more readily than that in the case of the 2-aminopyridine.

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Binz and R  th, Ann., 486, 95 (1931)
Heyden, Chem. Centralblatt, 1935, II, 2283
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Tchitchibabin, Chem. Centralblatt, 1915, I, 1066.

Reported by Otto Turinsky
April 28, 1937.

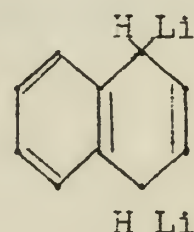
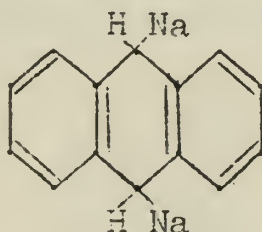
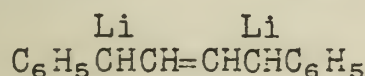
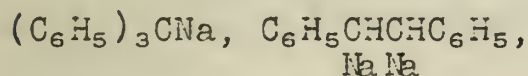
Ziegler, University at Halle
Morton, Massachusetts Institute of Technology

The last organo metallic compounds to become known were those of the alkali group. Special properties of these alkali organo metallic compounds give rise to new methods of synthesis which formerly were not possible.

All the important types of alkali organo compounds were isolated for the first time by Wilhelm Schlenk, who pioneered in this field twenty years ago. He also studied some of the reactions which this type of compound could undergo.

I. The Method of Preparing the Alkali Organo Compounds

(a) Metal addition to a radical, certain unsaturated hydrocarbons or aromatic hydrocarbons. The following substances have been prepared in this manner:



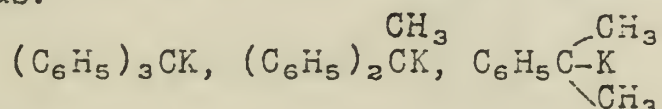
(b) By the use of mercury alkyls:



(c) Ether cleavage by a metal:



this reaction is best when R is tertiary, carrying at least one aromatic nucleus.



have been successfully prepared from the corresponding ether.

(d) Intermediates in the Wurtz-Fittig synthesis:



In order to obtain an alkali organo compound in this case it is evident that reaction (2) must proceed less readily than reaction (1). This deviation was noticed by Ziegler and Colonius in 1930 while working with Li alkyls and aryls.

Chemical Department of the University of California, Berkeley, California

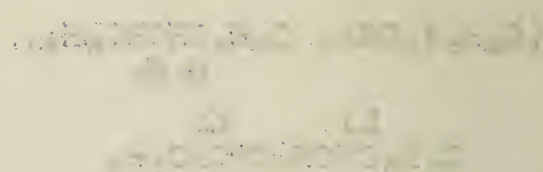
The first series of experiments was designed to determine the effect of the alkyl chain length on the rate of polymerization of methyl methacrylate in benzene solution at 60°C. The results are shown in Table I.

It is seen from Table I that the rate of polymerization increases with increasing alkyl chain length. This is in agreement with the results of other workers who have found that the rate of polymerization of methyl methacrylate increases with increasing alkyl chain length.

EXPERIMENTAL

Materials

The methyl methacrylate was purified by distillation under reduced pressure. The benzene was purified by distillation under reduced pressure. The alkyl chains were purified by distillation under reduced pressure.



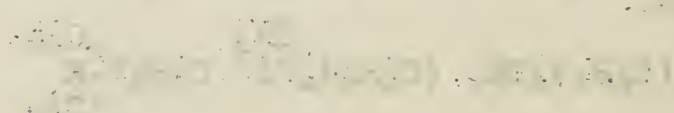
Procedure

The reaction was carried out in a 100 ml. round-bottomed flask.

The flask was equipped with a magnetic stirrer.

The reaction mixture was stirred for 1 hour at 60°C.

The reaction mixture was then poured into a large volume of water.



The polymer was then dried under vacuum at 60°C.

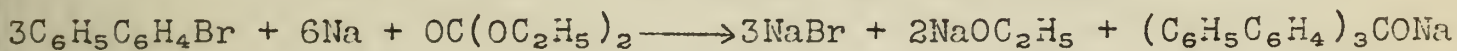
The polymer was then weighed and the weight of the monomer was determined.

The results are shown in Table I.

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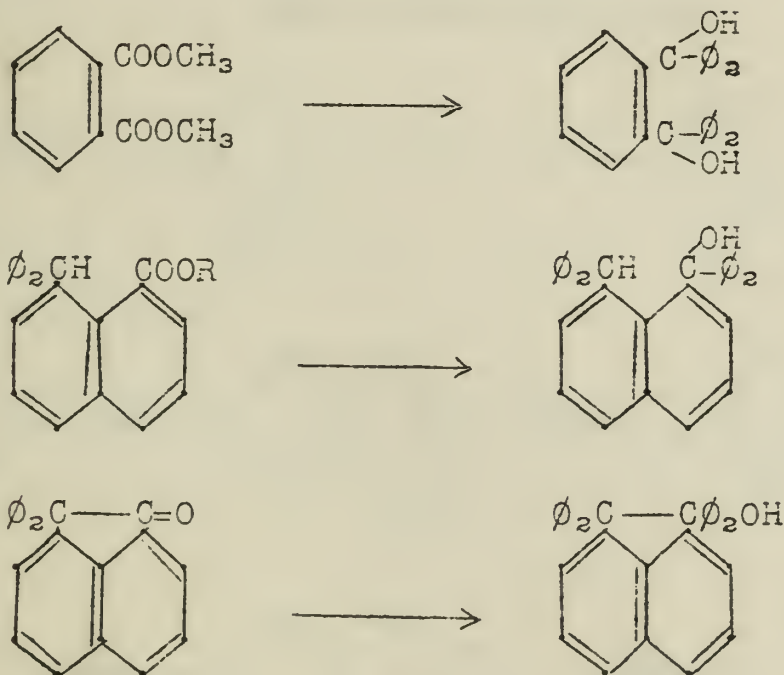
For its use in synthesis it is not necessary to isolate this compound as in the case of the Grignard reagent, as shown by these examples:



II. Addition of Alkali Organo Compounds to Carbonyl Groups. Comparison with Grignard Reagents

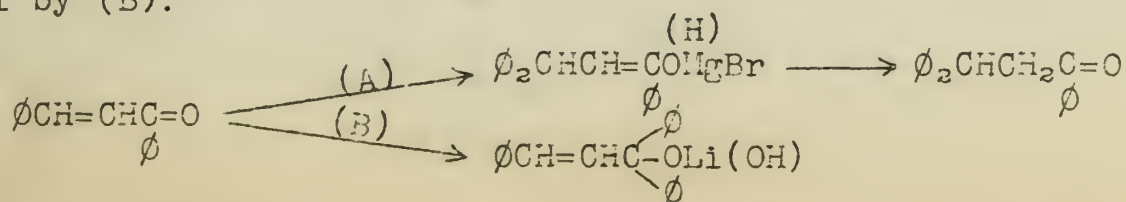
From an economical standpoint the above synthesis of aromatic sodium compounds, on account of its cheap starting materials, has a decided advantage over the Grignard synthesis. It is conceivable then that certain compounds could be prepared cheaply on a commercial scale by the use of sodium aryls. Use of the Grignard reagent in technical preparation of these compounds is not now feasible due to economical considerations.

Wittig has shown that certain carbonyl and carbalkoxy groups did not react with Grignard reagents but reacted smoothly with Li compounds.

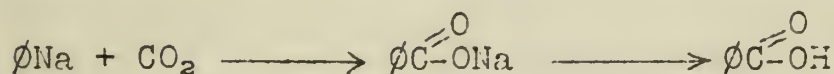
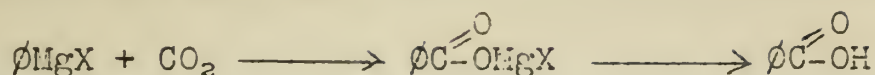


Fundamentally magnesium compounds differ in reaction from Li compounds:

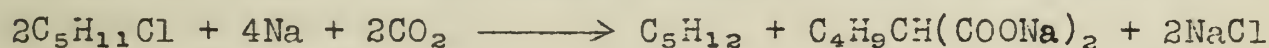
(a) Kohler in 1906 prepared phenyl diphenyl ethyl ketone by (A) whereas recently Luttringhaus prepared diphenyl styryl carbinol by (B):



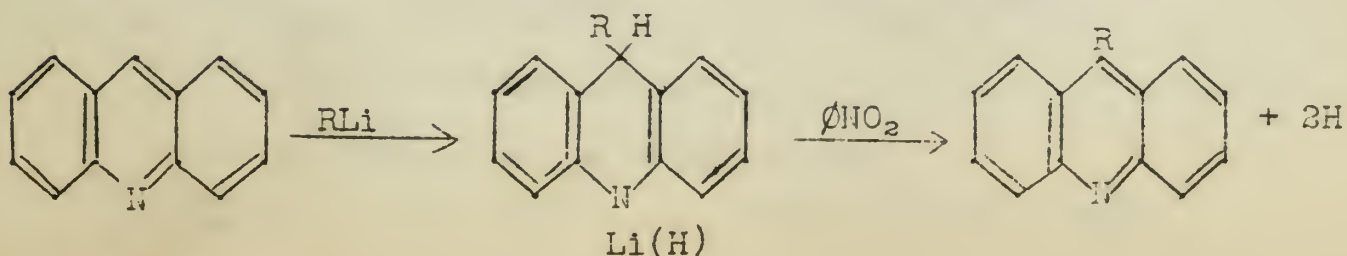
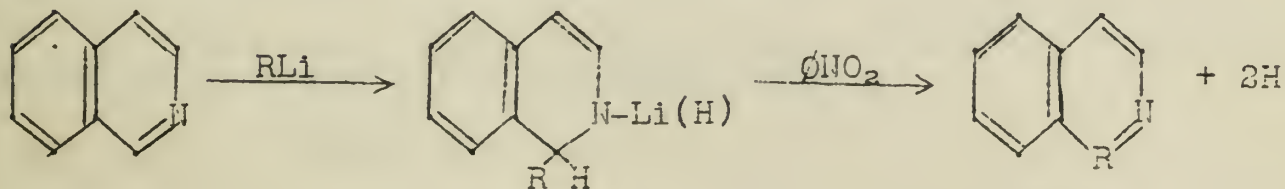
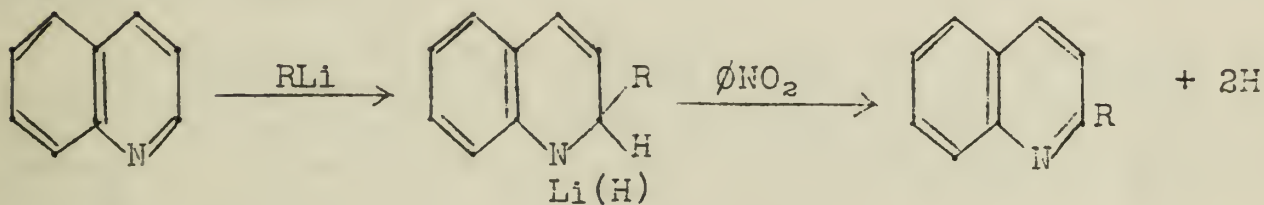
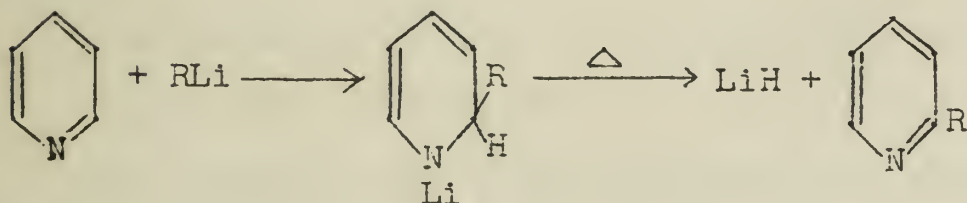
(b) Reaction with CO_2 :



Morton and coworkers have prepared a series of aliphatic acids by the reaction of the corresponding halogen compound, with sodium and carbon dioxide under pressure forming the expected monocarboxylic acid along with appreciable yields of substituted malonic acids.

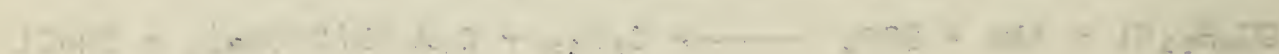


III. Alkali Organo Compounds with Pyridine and Similar Compounds



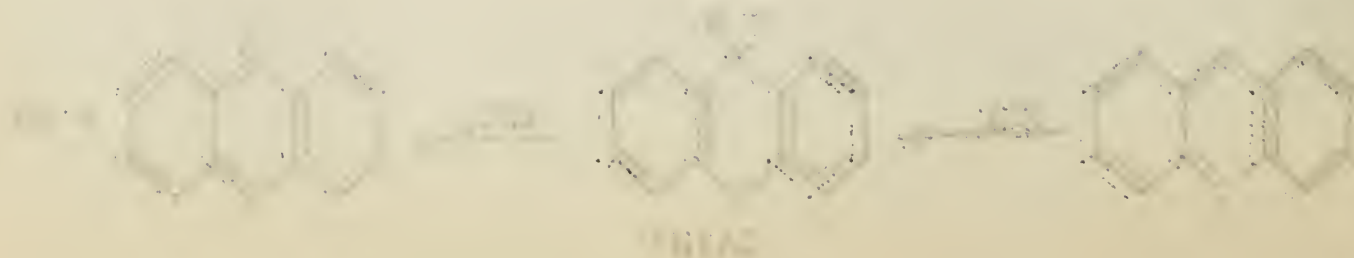
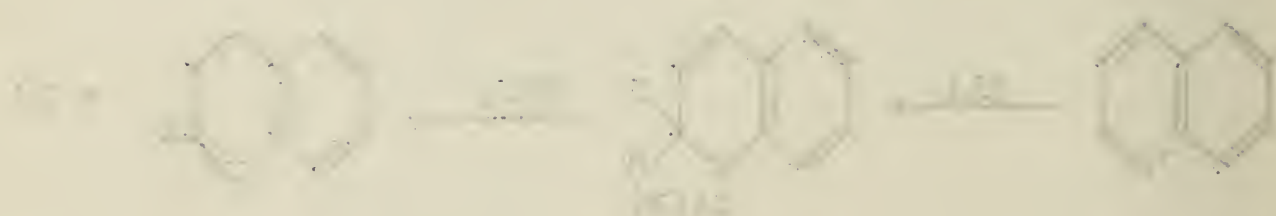
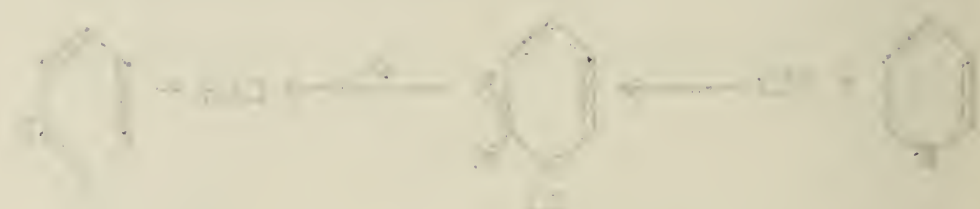


The above reactions are exothermic, indicating that the aromaticity of benzene is a stabilizing factor. The heat of hydrogenation of benzene is less than that of cyclohexene, which is a measure of the aromaticity of benzene.

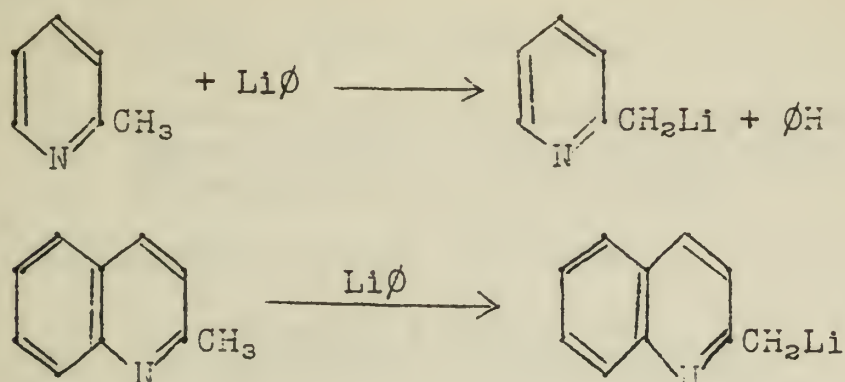


14.1.1.1. Reaction of Benzene with H_2

The reaction of benzene with H_2 is exothermic.

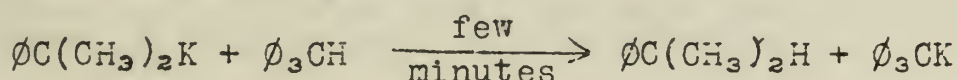


In α picoline and α quinaldine Li phenyl does not add to the N=C double bond but replaces one of the side-chain hydrogens:

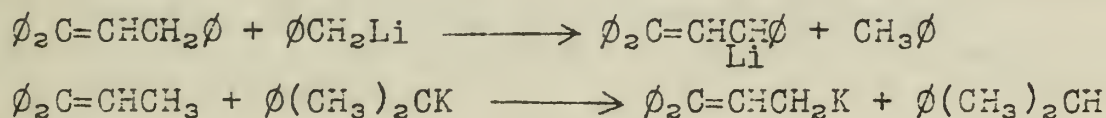


IV. Alkali Organo Compounds as Metal Carriers

Alkali metal alkyls can be used as carriers of the alkali metal to introduce it into other organic molecules depending on the nature of both components.



The analogous preparation of triphenyl Li methane by means of Li phenyl requires heating at 50-60° C. in a closed vessel for a few hours.



The speed of this double decomposition depends greatly on the reaction medium: ether accelerates, benzene or other hydrocarbons arrest the reaction.

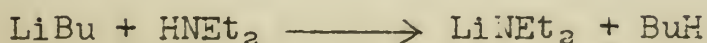
In the above reactions a concurrence was not possible between addition and substitution. However, if we allow an alkali alkyl to react with a carbonyl or cyanide compound containing a replaceable hydrogen in the α position we arrive at these generalizations: magnesium compounds generally add, sodium compounds substitute and lithium compounds take a middle position.

In cases where addition takes place, substitution can be effected as shown in the following example:

Normal addition:



Forced substitution:



V. Summary

I. Preparation:

a. Aryl alkali organo compounds:

1. Direct addition to certain structures.
2. Ether cleavage of aryl substituted ethers.
3. Intermediate in Wurtz-Fittig.

b. Alkyl alkali organo compounds:

1. Mercury alkyls and metal.
2. Intermediates in Wurtz-Fittig.

II. Comparison of Grignard reagents and alkali organo compounds:

- a. Lithium aryls are more sensitive to carbonyl groups.
- b. Lithium aryl compounds add 1,2 to α, β unsaturated ketones whereas phenyl Grignards add 1,4.
- c. Lithium aryls react with carbon dioxide to give ketones.
- d. Sodium and potassium alkyl and aryl compounds react with carbon dioxide to give carboxylic acids.

III. Reaction of lithium aryl and alkyl compounds with N=C double bond.

- a. Addition to pyridine and similar compounds followed by decomposition yields alkylated derivatives.
- b. In picoline and quinaldine replacement by metal of side-chain hydrogen.

IV. Alkali organo compounds as metal carriers:

- a. Ability to introduce alkali metal into organic molecules is dependent on both components as well as the reaction medium.
- b. Generally Grignard reagents add, sodium compounds substitute and lithium compounds take a middle course.

Bibliography:

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- Ziegler, Angew. Chem., 49, 455 (1936)

Reported by John W. Robinson

James H. Sample

May 5, 1937.

1. Introduction

2. Objectives of the Study

1. To determine the effect of the study on the population.
2. To determine the effect of the study on the population.
3. To determine the effect of the study on the population.

3. Methodology

1. Description of the study design.
2. Description of the study design.

4. Results and Discussion

1. Description of the study design.
2. Description of the study design.
3. Description of the study design.
4. Description of the study design.
5. Description of the study design.

5. Conclusion

1. Description of the study design.
2. Description of the study design.
3. Description of the study design.

6. References

1. Description of the study design.
2. Description of the study design.
3. Description of the study design.
4. Description of the study design.
5. Description of the study design.

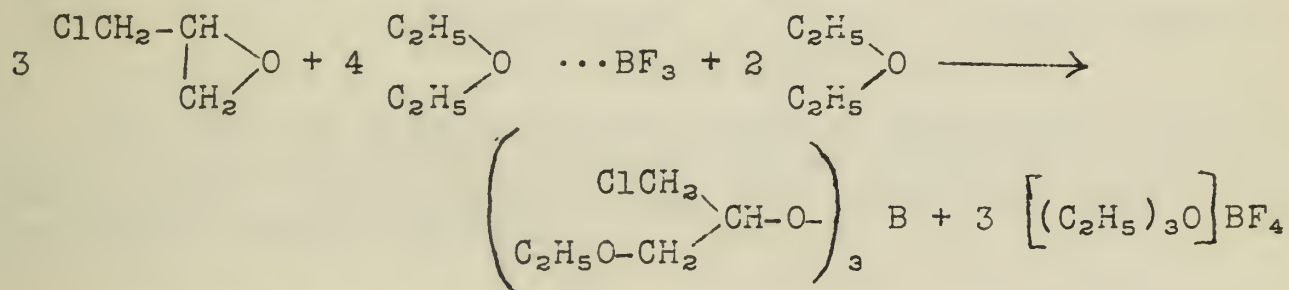
7. Appendix

1. Description of the study design.
2. Description of the study design.
3. Description of the study design.
4. Description of the study design.
5. Description of the study design.

Meerwein - University of Marburg

Attempts to prepare true tertiary oxonium salts of the general formula $[(C_nH_{2n-1})_3O]X$, corresponding to tertiary sulfonium and quaternary ammonium salts, have been made since the proposal of the oxonium theory by Collie and Tickle in 1899, but heretofore have failed.

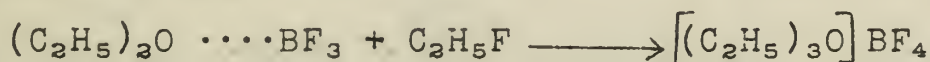
I. Preparation.--(1) The reaction which led to the discovery of the trialkyl oxonium salt consists of the action of the boron fluoride compound of ether on ethylene oxide or on epichlorohydrin:



Likewise, boron fluoride dimethyletherate reacts with epichlorohydrin in excess dimethyl ether to give the corresponding products.

Other metallic and non-metallic halides such as SbCl_5 - or SnCl_4 -etherate react with epichlorohydrin to give more or less stable tertiary oxonium salts.

(2) Boron fluoride etherate and ethyl fluoride react slowly at ordinary temperatures in the presence of ether to give the oxonium salt, the latter, being relatively insoluble in ether, precipitating out:



Ethyl fluoride adds much more rapidly to the boron fluoride compound of dimethyl ether with the formation of dimethylethyl oxonium boron fluoride.

By this simple method of preparing tertiary oxonium salts, other such salts may be expected by the addition of alkyl halides to metallic and non-metallic etherates. The addition of alkyl halides to other oxygen compounds, as well as to N-compounds, such as the di- and triaryl amines that do not readily add alkyl halides directly is now being studied. They have already established that CH_3Cl combines with the BCl_3 compound of dimethyl ether to give trimethyloxonium boron chloride $[(CH_3)_3O]BCl_4$.

Since alkyl halides do not add to ethers, it is assumed that the described reactions take place due to the ease of formation of the BF_4^- ion.

II. Properties.--(1) Salt-like in character.

(2) Colorless, fern-like crystals similar to NH_4Cl .

(3) In solubility, they correspond to the quaternary NH_4^+ salts. In general, they are soluble in nitrobenzene, liquid

THEORY OF THE EARTH

The first part of the theory of the earth is the study of the origin and development of the earth and its various parts. This includes the study of the earth's crust, the interior, and the atmosphere.

The second part of the theory of the earth is the study of the earth's surface features, such as mountains, rivers, and oceans. This includes the study of the earth's topography and the processes that shape the surface.

$$f(x) = \left(\frac{1}{2} \right)^x$$

The third part of the theory of the earth is the study of the earth's climate and weather. This includes the study of the earth's atmosphere and the processes that control the climate.

The fourth part of the theory of the earth is the study of the earth's life. This includes the study of the earth's plants and animals and the processes that control their distribution.

The fifth part of the theory of the earth is the study of the earth's resources. This includes the study of the earth's minerals, forests, and other natural resources.

THEORY OF THE EARTH

The sixth part of the theory of the earth is the study of the earth's history. This includes the study of the earth's past and the processes that have shaped it.

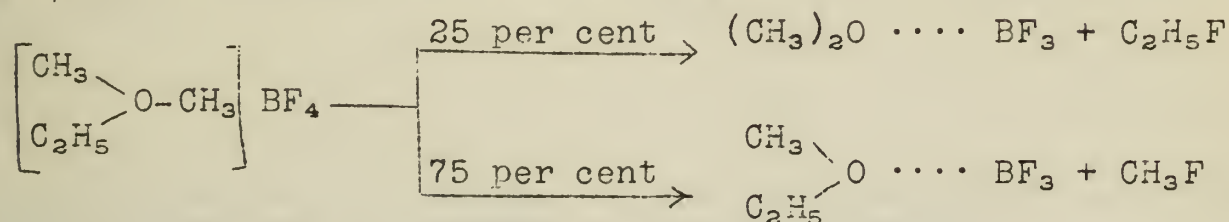
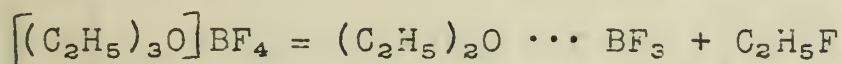
The seventh part of the theory of the earth is the study of the earth's future. This includes the study of the earth's potential and the processes that will shape it.

The eighth part of the theory of the earth is the study of the earth's present. This includes the study of the earth's current state and the processes that are shaping it.

The ninth part of the theory of the earth is the study of the earth's whole. This includes the study of the earth as a whole and the processes that control it.

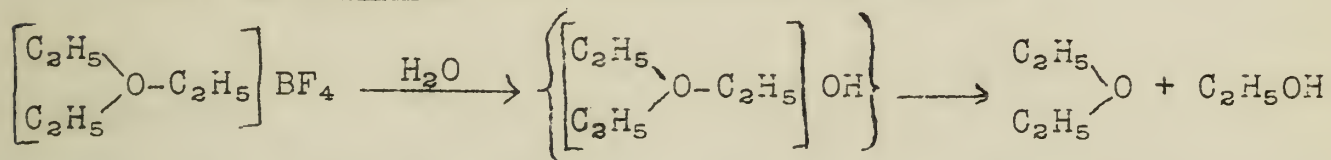
sulfur dioxide, nitromethane, methylene chloride and acetone; difficultly soluble to insoluble in other organic solvents.

(4) Their stability depends on their purity. Thermal decomposition proceeds as follows:

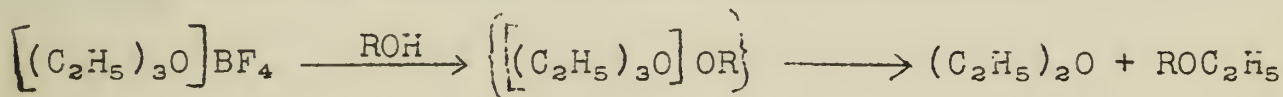


(5) They are extraordinarily reactive compounds, acting in double decomposition like the heteropolar inexistant fluoroboric ester $(BF_4)R$. They are, therefore, good alkylating agents, even surpassing dialkyl sulfates.

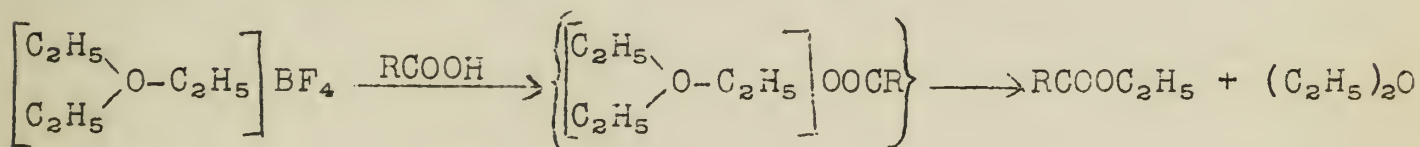
III. Reactions.--(1) Hydrolyzed by water:



(2) Alcohols and phenols are easily alkylated:



(3) Organic acids react to form esters:

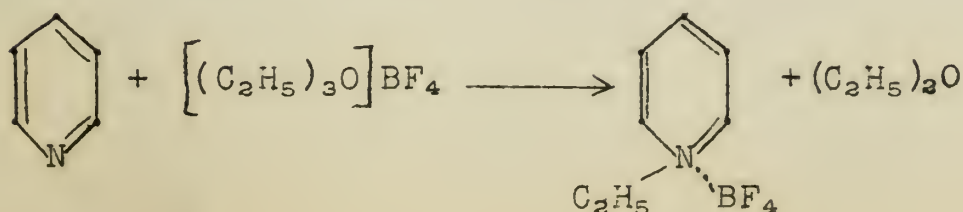


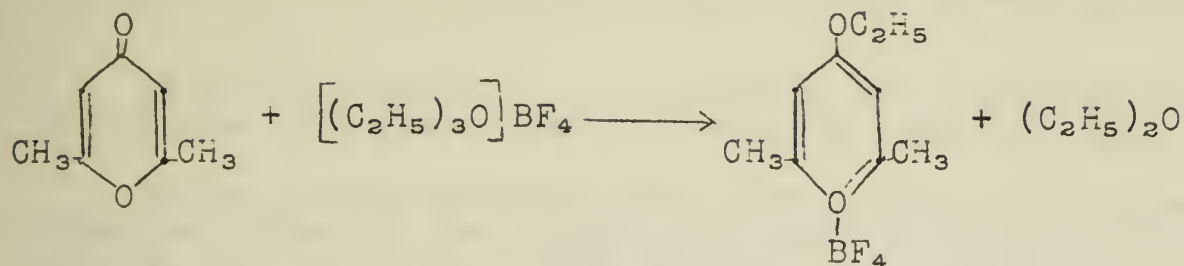
In this and in (2) alkylation takes place much more readily in alkaline solution.

(4) Malonic ester or acetoacetic ester may be alkylated.

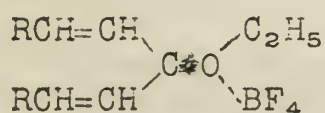
(5) Ammonia yields a mixture of mono-, di- and trialkyl amines, and the quaternary ammonium salt.

(6) Formation of other -onium salts:





α,β -Unsaturated ketones, such as dibenzalacetone, give intensely colored salts, probably of the type formula:



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Reported by R. L. Hicks
May 12, 1937.

The catalytic properties of finely divided metals were made prominent by Sabatier and his students, who observed the order of decreasing activity of the metals studied to be Ni, Co, Pt, Fe, and Cu.

Ni.--The preparation of an active reduced Ni by the process of Sabatier was difficult and the catalyst very sensitive to poisoning.

Raney in 1927 indicated the preparation of a rather stable Ni catalyst active at low temperatures and pressures by the attack of a 40-60 per cent Ni-Al alloy by NaOH. The catalyst was first made well known in 1932 by Adkins and his students who found it superior to the Ni on kieselguhr type of catalyst for the reduction of aldehydes, azobenzene, and benzonitrile, and equal to the supported catalyst in other reductions.

du Pont in 1936 reported selective reductions by Raney Ni not permissible with the platinum oxide catalyst. The $-\text{CH}=\text{CH}_2$ was more rapidly reduced than the $-\text{CH}=\text{CH}-$ group and substituted compounds of the type $\text{RR}'\text{CH}=\text{CH}_2$ and $\text{RR}'\text{CH}=\text{CHR}'$ were difficultly reduced or not at all. Double bonds in the benzene and furane rings were not reduced.

Paul and Hilly in 1936 indicated modifications in the technic of Raney allowing the preparation of the alloy without special furnace and avoiding the presence of Al in the final catalyst by treating the alloy with NaOH at a lower temperature and over a shorter period. They observed that alloys containing less Ni produced just as active a catalyst.

Delepine and Horeau found the hydrogenation of carbonyl compounds was greatly speeded up by the addition of small amounts of NaOH to the Raney Ni. For instance, while Adkins had reported the hydrogenation of acetone by Raney Ni in 11.2 hours, these workers found that Raney Ni plus 0.1 cc. 10 N NaOH allowed complete hydrogenation of 10 g. acetone in 30-40 minutes.

The favorable effect of alkalies had been noted in specific cases by previous workers. Carothers and Adams found it increased the rate of hydrogenation of benzaldehyde using the PtO_2 catalyst. Cake observed an alkaline medium necessary for the hydrogenation of glucose. I. G. Farbenind. recommended the presence of various alkalies in the hydrogenation of sugars. Hoffmann, La Roche and Company recognized the effect of alkalies in the hydrogenation of phenol, resorcinol, and homologs. Adkins and collaborators indicated the favorable effect of NaOH on the hydrogenation of the diethyl acetal of furfural. Kelbe used Ni in the presence of alkali for quantitatively removing halogen from organic compounds with hydrogen.

Delepine and Horeau also found the deposition of a small quantity of Pt on the surface of the Ni increased further its activity when a little NaOH was added. With methyl-ethyl ketone by the addition of 0.2 cc. 10 N NaOH to the Ni alone the reaction was speeded up four times and terminated in 72 minutes. Using platinized Ni the reaction was speeded up nine times and was

complete in 28 minutes. Other metals of the Pt family increased the velocity of hydrogenation in the same manner, osmium and iridium being as effective as Pt.

Ninety-six per cent ethyl alcohol was usually used as a solvent, although methyl alcohol, ether and alcohol mixtures, and water were effective where used. Other solvents were not tried.

The method was successfully applied to more than forty carbonyl compounds including saturated and unsaturated aliphatic and aromatic aldehydes and ketones, cyclic ketones, keto-alcohols, keto-acids, keto-esters, and a few ketoses and aldoses.

Cu and Co as Hydrogenating and Dehydrogenating Catalysts.--
Faucounau obtained active copper by the action of NaOH on a commercial alloy containing fifty per cent Al, forty-five per cent Cu and five per cent Zn. For dehydrogenation this catalyst had an activity comparable to that of the Cu of Sabatier and was more stable. Dehydrogenation of primary alcohols occurred most rapidly at 270-300°, of secondary alcohols at 250°.

For hydrogenation the catalyst behaved similar to reduced Cu saturating the carbon to carbon double bonds at the end of the chain. It transformed aldehydes and ketones easily to the corresponding alcohols at temperatures varying from 125-150°. The reaction was about three times more rapid in the presence of dilute NaOH. Only double bonds in α -position were saturated. The benzene nucleus and cyclic double bonds were not attacked.

Faucounau also obtained active Co by the action of NaOH on Co-Al alloy. As a dehydrogenating catalyst it possessed an activity slightly superior to that of Cu, requiring somewhat lower temperatures.

As a hydrogenating catalyst it presented an activity at least equal to that of reduced Co from cobalt nitrate. At 100° it permitted the saturation of double bonds and the transformation of aldehydes and ketones into the corresponding alcohols. Between 175° and 200° the benzene nucleus was reduced.

With benzene derivatives at 100° only saturation of the side-chain was obtained, while at 200° the nucleus was also completely saturated.

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Reported by Velma E. Nichols
May 12, 1937.

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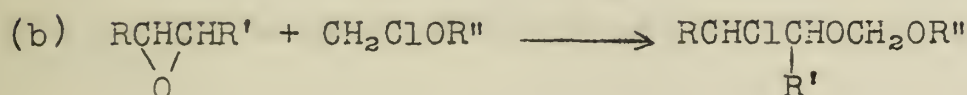
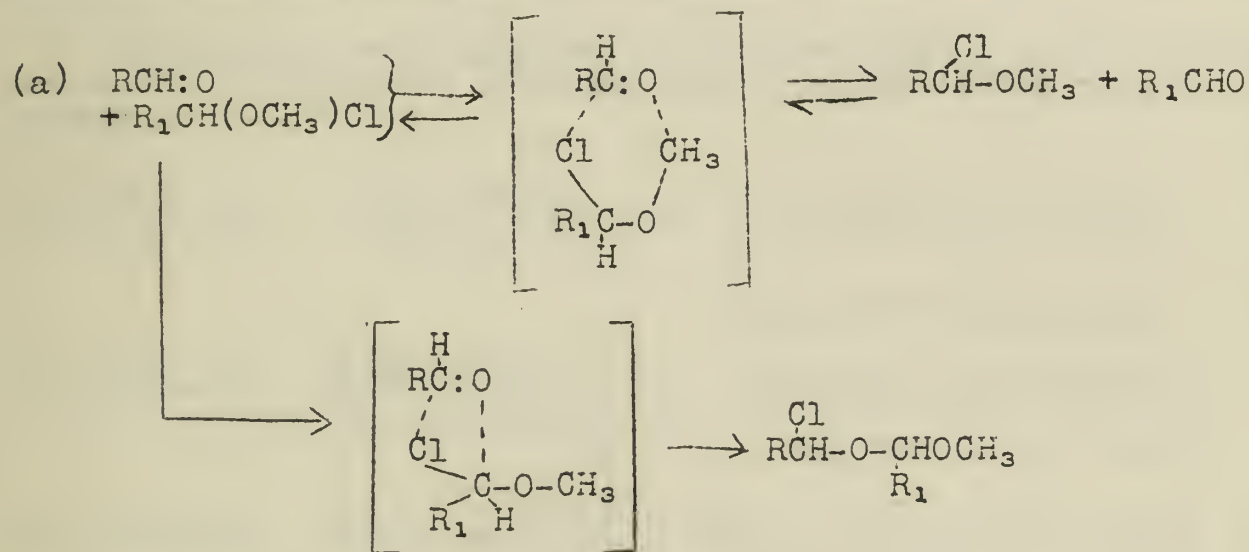
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ADDITION OF α -CHLORO-ETHERS TO OLEFINE DOUBLE BONDS

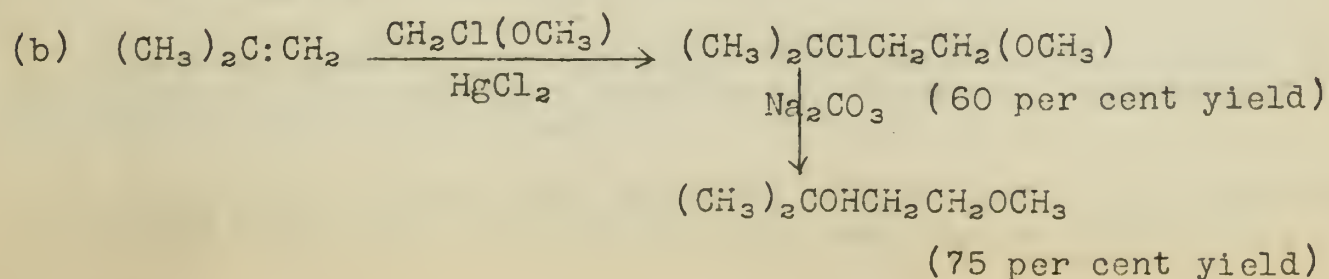
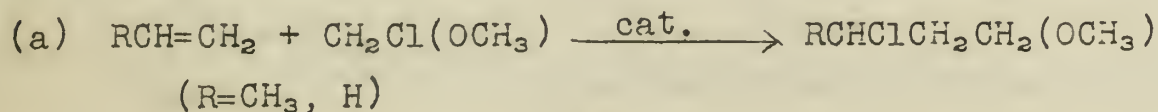
The possibility of alkylating unsaturated hydrocarbons through the addition of alkyl halides to their $C=C$ double bond has been suggested many times. An endeavor has been made to carry over the process of the Friedel-Crafts Reaction to aliphatic unsaturated systems. It is well known that the alkylation of keto-enol-tautomers is traced to the double bond of the enol form.

α -Chloro-ethers may be regarded as highly activated alkyl halides as the methoxy group does not enter into the addition reactions. α -Chloro-ethers may be added directly to the unsaturated hydrocarbon, or the hydrocarbon may be treated with an alcohol, HCl , and an aldehyde as will be observed in the reactions below. Catalysts such as $HgCl_2$, $ZnCl_2$, $SnCl_4$, and $SbCl_5$ are used. The first mentioned catalyst seems to be the most general one, however, in certain additions it is surpassed by others. Catalysts are not necessary to obtain addition. However, the yields are very much improved by their presence.

Among some of the earlier reactions of α -chloro-ethers observed are the following of interest here:



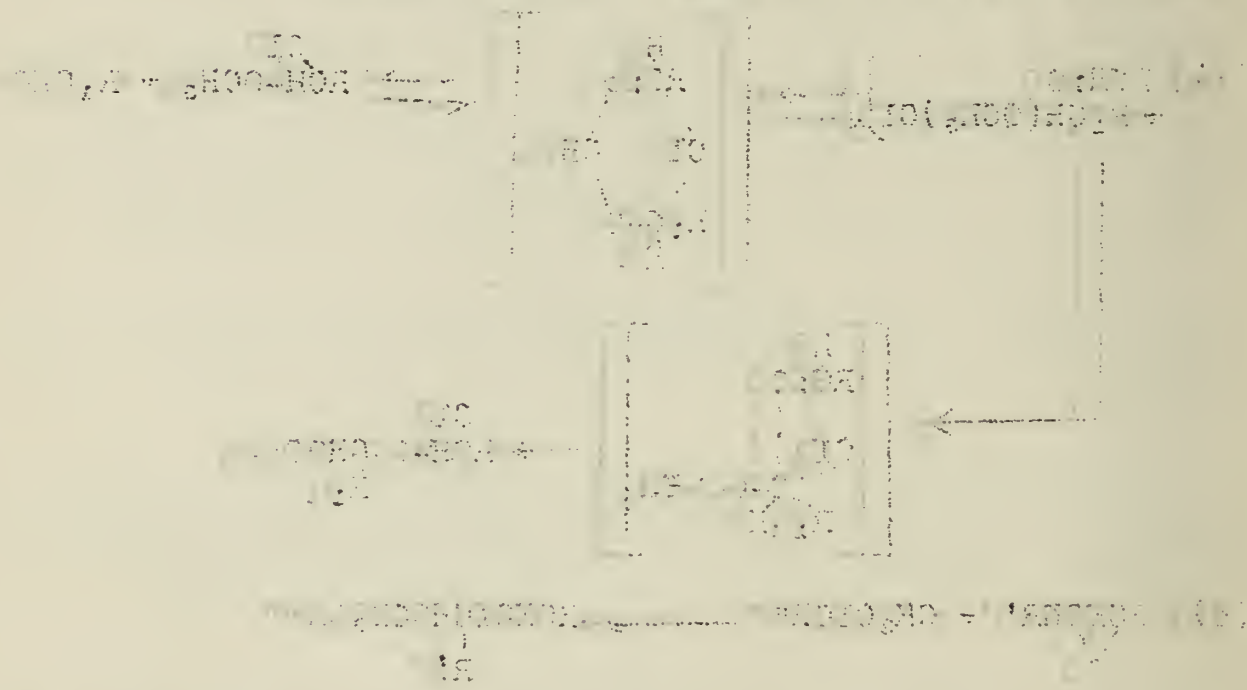
The following reactions have been carried out with unsaturated hydrocarbons.



The purpose of this study was to determine the effect of the administration of a certain drug on the blood pressure of patients with hypertension. The study was conducted over a period of six months, during which time the blood pressure of 100 patients was recorded at intervals of one week. The results of the study are as follows:

The first group of patients, consisting of 50 individuals, received the drug in question. The second group, consisting of 50 individuals, received a placebo. The blood pressure of the first group was recorded at intervals of one week, and the results were compared with those of the second group. The results of the study are as follows:

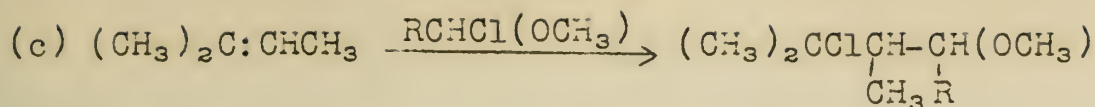
Among the patients who received the drug, the following results were obtained:



The results of this study indicate that the administration of the drug in question has a significant effect on the blood pressure of patients with hypertension. The drug appears to be effective in lowering blood pressure, and the effect is sustained over a period of 12 weeks.

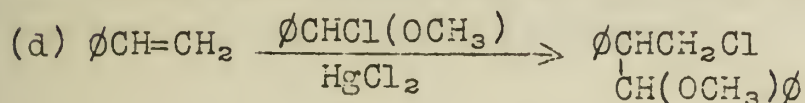
The following table shows the mean blood pressure of the patients in each group at the end of the study:

Group	Mean Blood Pressure (mm Hg)
Control Group	150
Drug Group	90

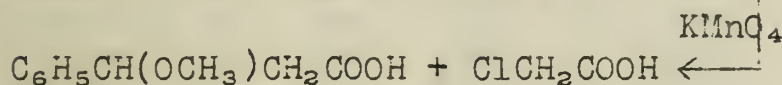
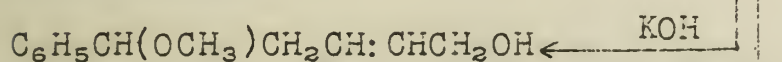
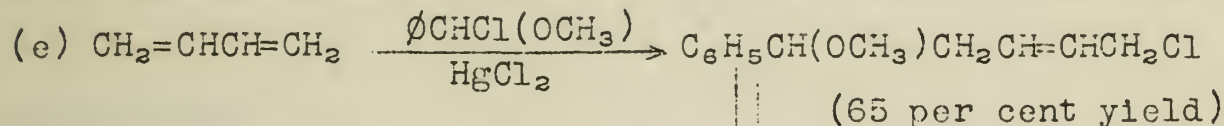


(R=∅; with catalyst, 65 per cent yield, no catalyst, 17 per cent yield)

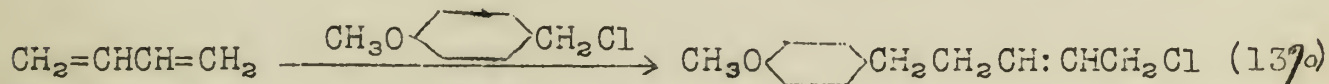
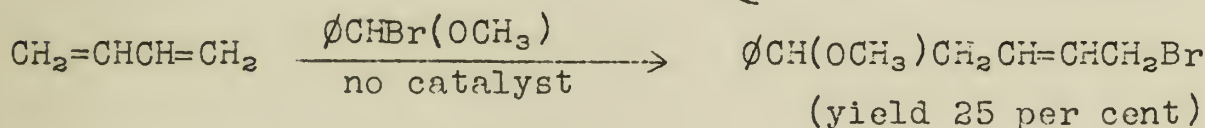
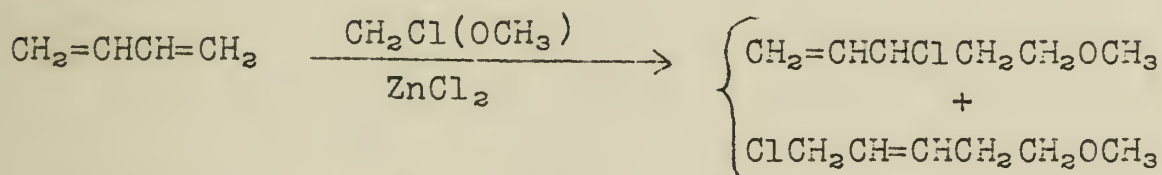
(R=H; with catalyst, 40 per cent yield)



Cyclohexene and 1,2-dihydronaphthalene react similarly. 2,3-Dihydronaphthalene does not give an addition product.



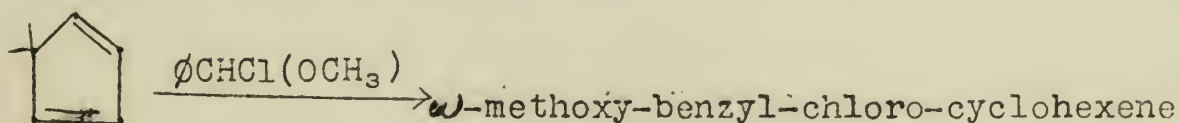
Butadiene, benzaldehyde, hydrogenchloride, methyl alcohol, and mercuric chloride give the same product in 20-25 per cent yields.



Similar yields were obtained using $SnCl_4$, $SbCl_5$, or $HgCl_2$ as catalyst.

Dihydrobenzene gave similar reactions, with the various chloro-ethers, but the products were not identified.

(f)



Only one product was obtained. The reaction was slower in the absence of the catalyst than in its presence. The method of addition was not determined.

It will be noticed that somewhat higher yields are obtained with $\emptyset CHCl(OCH_3)$ than with $CH_2Cl(OCH_3)$ showing an activating

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effect of ϕ on the C-Cl linkage. The addition of p-anisyl chloride is particularly interesting as it shows the activating effect of the methoxy group through a vinylogous system. It was thought that triphenyl chloromethane would add, but it did not, probably due to steric hindrance.

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Reported by S. O. Greenlee
May 19, 1937.

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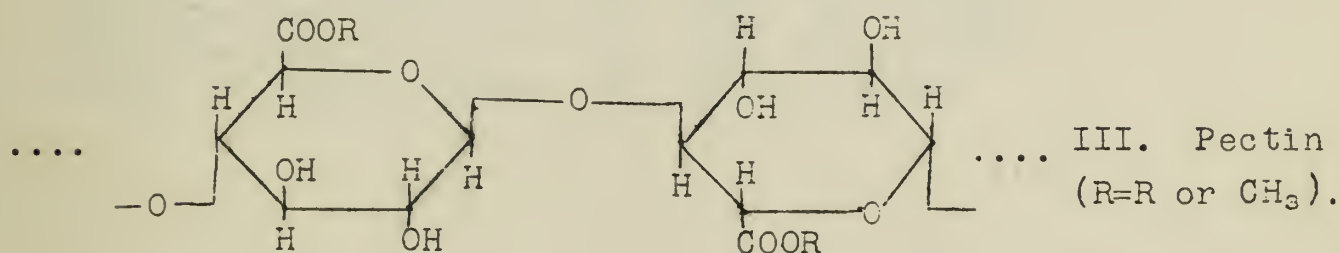
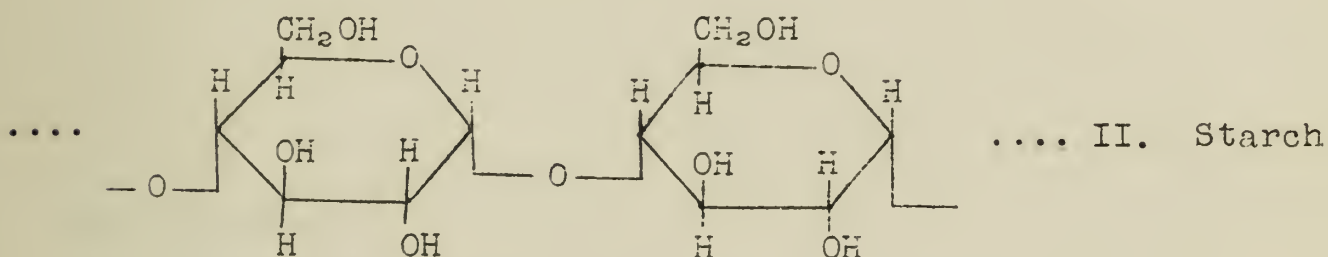
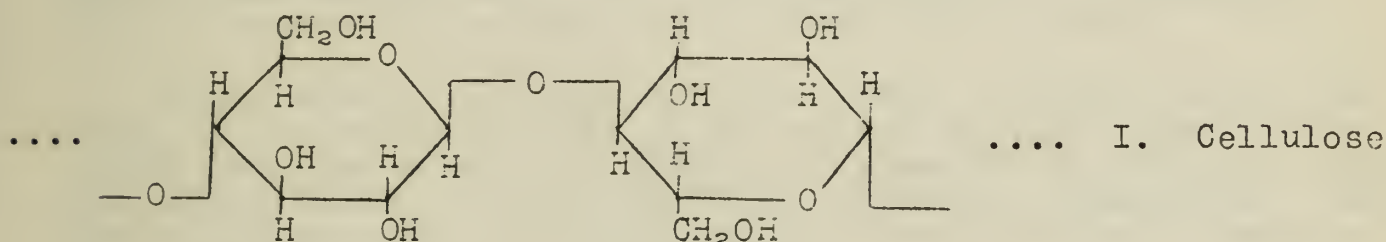
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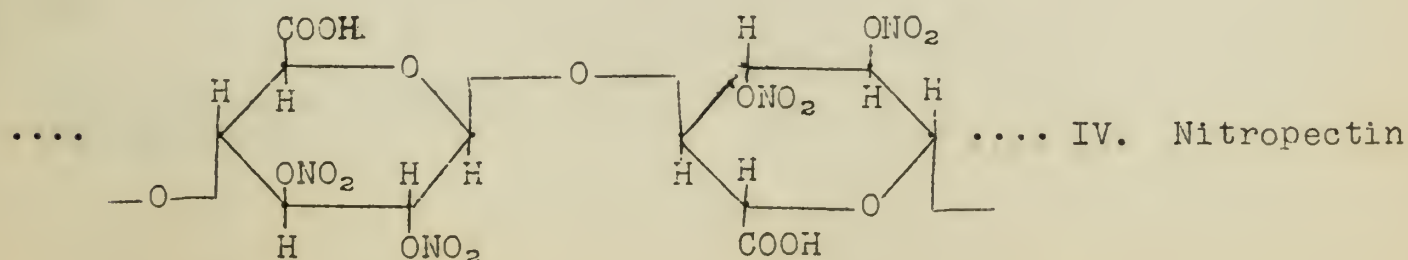
PECTINS AND THEIR ESTERIFICATION

It has been known that pectins, a principal constituent of the plant cell materials, on degradation, yield principally galactose derivatives and methyl alcohol. Ehrlich in 1929 concluded that pectin was formed around a framework of tetragalacturonic acid, either in a large ring or an open type structure.

In conjunction with X-ray data, it is proposed that pectin should consist of galacturonide chains, similar to starch and cellulose (α - and β -glucopyranose polymers, respectively) in a formal manner as seen by the formulas:



Chemical evidence for the similarity of cellulose and pectin, heretofore lacking, was found in the properties of nitrocellulose and "nitropectin":

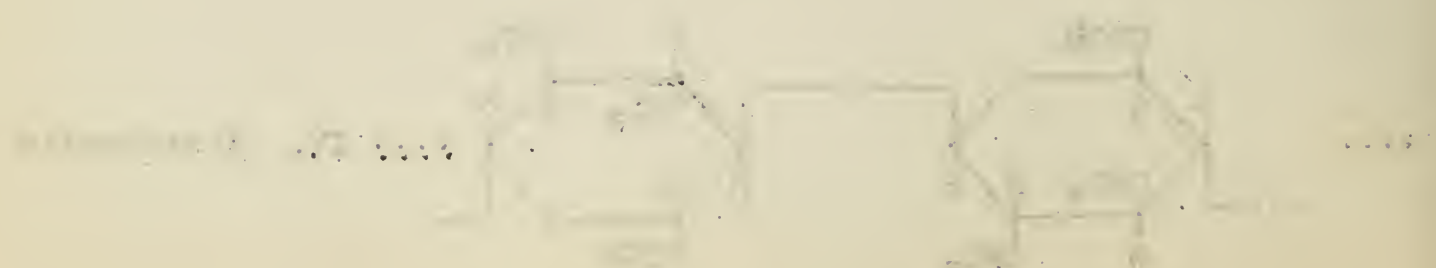


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The preparation and properties of the corresponding acetyl and formyl esters of pectin coincided with those of cellulose. These derivatives of pectin were easily prepared by direct acetylation or formylation of nitropectin.

The somewhat colloidal nature of pectin itself prevents accurate M. W. determinations. M. W. obtained by the Staudinger viscosity method, and further substantiated by osmotic measurements, indicate a chain of 100-350 galacturonic acid units in nitropectin, which was prepared directly from sugar beets. The exact chain length and M. W. of pectin cannot be determined closely because it is easily hydrolyzed and degraded.

The presence of a free carboxyl group in pectin esters was shown by the susceptibility of the esters to basic dyes. Films formed from the esters are similar in strength to cellulose films and show a linear orientation of the molecular components. These facts further point to a "stretched" linear polymeric configuration of pectin as illustrated in III.

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Schneider and Fritschi, Ber., 69B, 2537 (1936)
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Reported by A. G. Sharp
May 19, 1937.

In general, viruses include submicroscopic disease-producing agents. They have the distinguishing features of invisibility and failure to grow on the lifeless media ordinarily used for bacterial reproduction. Until recently the lack of any suitable methods of study has kept us ignorant of the true nature of all these pathogens, both a living and a non-living character being indicated by the indirect evidence at hand.

Over a dozen human diseases are known to be caused by viruses, including smallpox, warts, yellow fever, poliomyelitis and rabies. Other diseases such as measles, mumps and chicken pox are thought to be due to viruses, but their etiology has not been proved definitely. Methods of immunization for some diseases, notably smallpox, have been developed; for this disease the active cowpox virus, closely related but less virulent, is inoculated. A good method used for prevention of yellow fever involves the use of a mixture of the active virus with an equal amount of its anti-virus, which has been formed in an animal. This union is broken in the human, liberating the active pathogen slowly enough that the body is able to develop an immunity without danger of developing an active case of the disease.

Viruses have so far been cultured only in the presence of living cells. Pasteur first reproduced animal viruses by passage through previously immunized animals, recovering the virus in increased amount from the blood of the animal after a few days. Formerly viruses were cultured in vitro by incubating them with minced fresh tissue; however, growth was not good. The method now in use is to incubate a hen's egg for ten days, cut a hole in the shell over the air sac, inoculate with the virus the chorioallantoic membrane immediately inside the sac, seal the egg and incubate. The virus develops very well on this medium.

Literally hundreds of plant diseases have been attributed to viruses. Transmission occurs commonly through sucking insects; contact of a healthy plant with the sap of a diseased plant in many cases causes infection. Methods of immunization have not been developed for plant diseases, and if developed would probably be impracticable since the sheer number of plants usually involved would make their cost prohibitive. The problem of the plant pathologist is largely one of controlling or eradicating the vector of infection.

In the study of plant viruses most of the detailed work has been carried out on the virus of the mosaic disease of tobacco, because of its ready availability, its high infectivity and its stability. Vinson¹ was the first to show that the virus was nitrogenous and could be worked with successfully from a chemical standpoint. On the basis of this indication and with improved methods for working with proteins Stanley² has isolated from mosaic-diseased plants a crystalline protein possessing the properties of the virus. Briefly, Stanley extracts the chopped tobacco plants with sodium phosphate solution and precipitates the virus and contaminating proteins with ammonium sulfate. The solution of the proteins in sodium phosphate is passed through a layer of diatomaceous earth on a filter; this material absorbs

the virus. The process of solution and reprecipitation is continued until a practically homogeneous virus precipitate is obtained. The molecule has also been directly precipitated from infected plant juice in the ultracentrifuge.³

The first announcement of this isolation was greeted by the objection that the true virus must actually be adsorbed on the crystalline protein, but Stanley⁴ has recently presented strong evidence that the virus and the protein are identical. Solutions of mixtures of the protein with tobacco proteins, egg albumin and other low molecular weight proteins were ultracentrifuged. The activity was entirely concentrated in the precipitate of high molecular weight protein, showing that the virus activity is not due to an agent which may be separated from the high molecular weight protein and transferred to other proteins. Virus solutions were centrifuged at their isoelectric points and when negatively and positively charged, and the activity of the supernatant liquids was studied. In all cases the virus activity of different portions of the supernatant fluids was proportional to the amount of high molecular weight protein present, demonstrating that at different hydrogen ion concentrations the virus activity cannot be separated from the high molecular protein. Of course, the fact that in all the manipulations made in other studies on the virus no separation of the protein and the virus has ever been observed is further evidence of their identity.

Since this most important contribution by Stanley, the isolation of the crystalline virus, rapid advances have been made by him and others in the study of its structure and, although the picture is by no means complete, its outlines are rather clear. The protein contains 16.5 per cent nitrogen, about 50 per cent carbon and 7 per cent hydrogen. The sulfur and nucleic acid phosphorus contaminants in the ordinary preparation can be removed by dialysis.⁵ Ultracentrifuge data^{3,6} show a molecular weight of 17,000,000, a value much larger than previously known for a protein.

The crystals obtained by Stanley averaged only 0.02-0.03 mm. in length. Best⁷ lately found that fibers of the protein several millimeters in length were deposited from the juice of diseased tobacco plants on standing in the cold for several months. On slight agitation the fibers broke into invisible pieces, but reformed again on standing. Best was of the opinion that Stanley's product probably consists of these mesomorphic fibers, held together by mild forces between structural units, rather than true crystals.

Takahashi and Rawlins⁸ early demonstrated that tobacco mosaic virus particles in solution showed the phenomenon of stream double refraction when observed between crossed nicol prisms. This occurs when rod-shaped particles in solution are brought into alignment by a current in the solution. Highly purified virus solutions separate on standing into two layers. The lower shows the phenomenon of stream double refraction, behaving as if composed of liquid crystals, while the upper is found to flow more easily in one direction than another. Solutions of the protein can be readily oriented by electric currents. All these physical properties point to a rod-shaped virus particle.⁹

X-ray patterns show about the same order of complexity as that produced by the keratin in feathers, with a repeat unit of $3 \times 22 \text{ \AA}$, 22 \AA being roughly the diameter assigned by Svedberg to the globular protein unit of molecular weight 36,000 which so frequently occurs in proteins. Other considerations combine with these to give us the crude but at least suggestive picture of a somewhat triangular rod, about 1000 \AA in length and 100 \AA in width, built up of regularly repeating protein units, themselves composed of folded polypeptide chains.

Many cases of change in the symptoms due to tobacco mosaic virus have been observed, indicating that spontaneous mutations had taken place in the virus molecule, giving rise to new strains.¹⁰ This suggests a close relationship to genes,¹¹ which for a long time have been thought to be protein units. Both viruses and genes are inactivated or caused to mutate by the same x-ray and ultraviolet bands, which suggests that alterations involved are similar. Both are incapable of reproduction outside living cells; both influence physical characteristics in their hosts. The virus differs from the gene in being able to move from cell to cell and in being inoculable into healthy plants.

Several other less stable plant viruses beside the tobacco mosaic have been obtained in crystalline form by ultracentrifugal precipitation.¹² And recently an animal virus, a stable protein causing warty growths on western cottontail rabbits, has been similarly isolated.¹³ Its molecular weight is more than 20,000,000.

This repeated isolation of protein viruses does not mean that all submicroscopic pathogens are protein molecules. In fact, the filterable agent causing the well-known Roux chicken sarcoma has been shown to be lipoidal.¹⁴ And it may well be that some diseases are due to living bacteria below microscopic size.

The properties of the virus protein tend to make non-existent the boundary between the living and non-living, for, although the protein can reproduce, grow and be inactivated, as can living things, it is still a protein molecule and may be considered non-living. By what means it reproduces is unknown, but it appears to be able to direct the metabolism of the host to produce not normal protein but more of the virus protein. Disease may be regarded as the disruption of normal metabolism caused by production of the virus protein.

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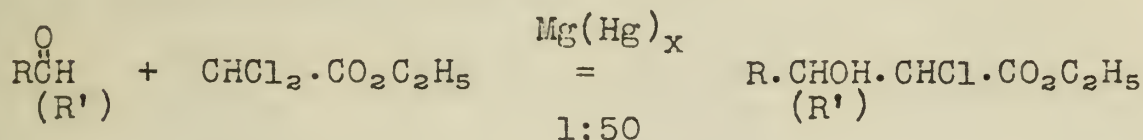
Reported by E. J. Matson
May 26, 1937..

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A New General Method of Preparing α -Chloro- β -hydroxy Esters.

G. Darzens has developed a new general method for the preparation of these esters by condensing dichloroacetic ester with aldehydes and ketones using dilute metal amalgams. The type reaction is:



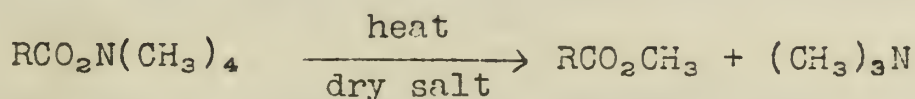
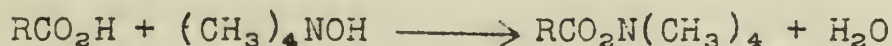
The reaction is very general and is said to be applicable to all aldehydes and ketones; R and R' may be aliphatic, aromatic or hydroaromatic. The dilute magnesium amalgam may be replaced by one of calcium or zinc. Either benzene or ether may be used as a solvent. The aldehyde or the ketone mixed with the dichloroacetic ester is added directly to the amalgam; the reaction is complete in 6-10 hours with stirring.

The yields obtained are 90 per cent or better.

Lactams from Lactones.--Späth and Lintner have recently reported the formation of lactams from lactones by the use of liquid ammonia in sealed tubes. Formerly it was thought that only lactones in which the hydroxyl group in the opened form was tertiary or secondary and unsaturated had the ability to form lactams in this manner. At low temperatures the lactone is opened and an amide is formed but at rather high temperatures, around 280° , lactams are formed. The yields varied from 55-90 per cent.

Preparation of Methyl Esters of Difficultly Esterified Acids.--Prelog and Piantanida have developed a new method for the preparation of the methyl esters of difficultly esterified acids which consists in the thermal decomposition of tetramethylammonium salts.

The tetramethylammonium salt is prepared by titrating the acid in methyl alcohol solution with a methyl alcohol solution of tetramethylammonium hydroxide using phenolphthalein as an indicator. The methyl alcohol is then evaporated and the salt decomposed under diminished pressure by cautious heating.



In the examples given, the yields varied from 71-95 per cent for the purified esters.

A New Preparation of Aldehydes.--Darzens and Levy and more recently Meyer have shown that the pyrolysis of α -ethoxy acids gives aldehydes in good yields. The method is especially applicable for certain high molecular weight aldehydes such as

A full description of the various types of the disease is given in the accompanying table. The disease is characterized by a high fever, a rapid pulse, and a general prostration. The disease is usually fatal, but in some cases it may be cured by the use of the following remedies.

1. *Salicylic acid* (10 grains) in water (1 ounce).
2. *Aspirin* (10 grains) in water (1 ounce).
3. *Acetylsalicylic acid* (10 grains) in water (1 ounce).

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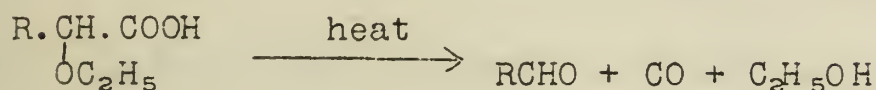
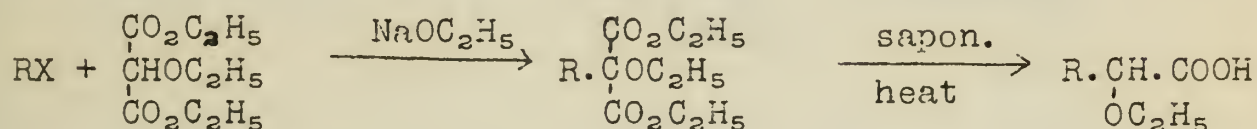
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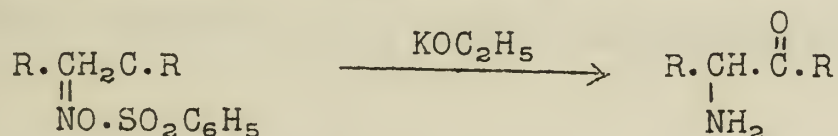
$\text{CH}_3(\text{CH}_2)_9\text{CHO}$, $\text{CH}_2=\text{CH}(\text{CH}_2)_9\text{CHO}$, $\text{CH}_3(\text{CH}_2)_{15}\text{CHO}$, $\text{C}_6\text{H}_5\text{CH}=\text{CH}.\text{CH}_2\text{CHO}$

The best method for the preparation of the α -ethoxy acids is by means of ethoxy malonic ester.

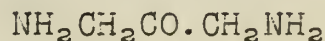
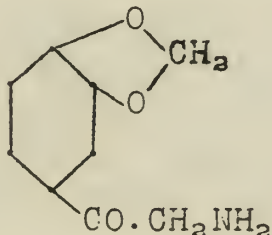
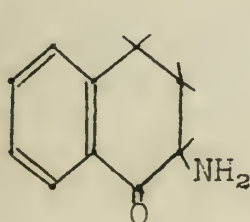


The temperature of the decomposition is $280-300^\circ$. The yields are generally above 70 per cent.

A New General Method for Obtaining α -Amino Ketones and α,γ -Diamino Ketones.--Neber and coworkers have shown that the saponification of the sulfonic esters of ketoximes (I) by potassium ethoxide does not lead to amides by a Beckmann rearrangement but rather gives α -amino ketones (II) independently of the sterical configuration of the oxime:

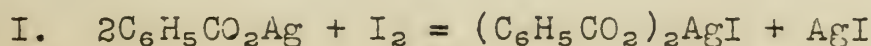


They have applied the reaction to the synthesis of such compounds as $\text{C}_6\text{H}_5\text{CH}.\text{CO}.\text{CH}_3$, $\text{CH}_3\text{CO}.\text{CH}.\text{CO}.\text{NH}.\text{C}_6\text{H}_5$, $\text{CH}_3\text{CO}.\text{CH}_2\text{NH}_2$



It is a rather general reaction for ketones of the type $-\text{CH}_2\text{CO}-$. However, in a few of the compounds tried, the reaction did not work. The yields in the final hydrolysis are good, varying between 70 and 94 per cent.

Preparation of α -Glycols and Iodoacetylenes.--It has been shown that iodine reacts with silver benzoate in suspension in benzene as follows:



The first part of the paper is devoted to a general discussion of the problem of the existence of solutions of the system of equations

$$\begin{aligned}
 & \frac{dx}{dt} = f(x, y, z), \\
 & \frac{dy}{dt} = g(x, y, z), \\
 & \frac{dz}{dt} = h(x, y, z),
 \end{aligned}$$

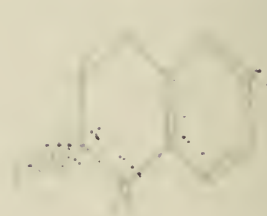
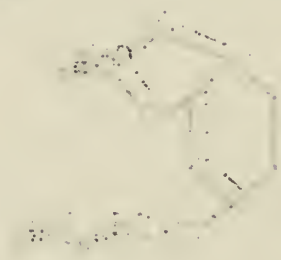
where f, g, h are continuous functions of x, y, z in a certain region.

The second part of the paper is devoted to a study of the properties of the solutions of the system of equations.

In the third part of the paper, the author considers the problem of the stability of the solutions of the system of equations.

$$\begin{aligned}
 & \frac{dx}{dt} = f(x, y, z), \\
 & \frac{dy}{dt} = g(x, y, z), \\
 & \frac{dz}{dt} = h(x, y, z),
 \end{aligned}$$

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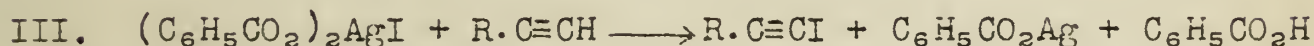
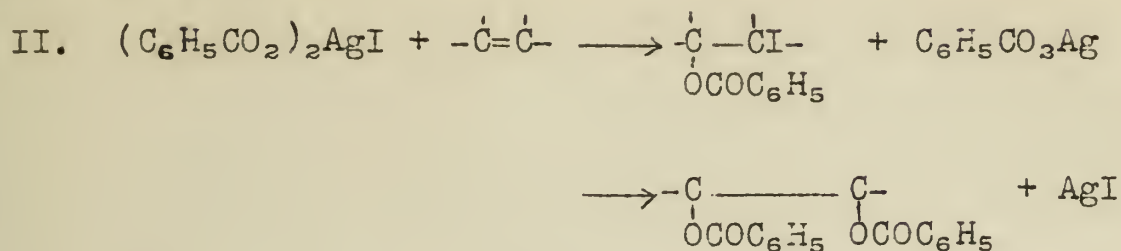


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$$\frac{dx}{dt} = f(x, y, z), \quad \frac{dy}{dt} = g(x, y, z), \quad \frac{dz}{dt} = h(x, y, z)$$

This complex iodo silver benzoate reacts with olefinic bonds and with acetylenes:



The olefin bond may be in R.CH=CH_2 (90 per cent), $\text{R}_2\text{C=CH}_2$, R.CH=CH.R , $\text{R.CH=CH.CO}_2\text{C}_2\text{H}_5$ (30 per cent), $\text{R.CH=CH.CH}_2\text{OCOR}$ (70 per cent), or in a cyclic olefin. The R groups may be aliphatic or aromatic. Iodine may be replaced by chlorine or bromine and the silver benzoate by silver acetate.

The final products from reaction II. may be saponified easily to give α -glycols. By this manner, 1-phenyl glycerol, $\text{C}_6\text{H}_5\text{CHOH.CHOH.CH}_2\text{OH}$, was first prepared in the crystalline form.

Trans addition to the olefin is preponderant or exclusive.

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